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RARE EARTH RESEARCH

Recent interesting rare earth research developments

a report by LINDSAY

We are frequently fascinated by the imagination of researchers who are working with the rare earths. It appears that technical people, observing the many essential uses of rare earth salts in chemical and industrial processes, are looking at these fifteen unique elements as a fertile field for exploration.

During recent years, rare earths have been accepted as basic chemical tools in a wide cross section of American industry. This suggests that fruitful results may be expected from the rare earth research projects currently being carried on in industrial laboratories and pilot plant operations from coast to coast. Here, for instance, are half a dozen which may interest you.

MILES OF MISCH. This isn't a new application, but we're wondering if you know that misch metal (an alloy of the mixed rare earths) is available in wire form as well as in ingot and rod form? Cerium alloys can also be had in powder form; they are used as getters in vacuum tubes. We don't make the metal, but we can put you in touch with those who do.

FLAME SPRAYING. A new process for flame spraying various refractory oxides on metallic surfaces has been brought to near completion. Titania, zirconia and alumina can be flame sprayed, but the thing that interests us is that flame sprayed cerium oxide has some unusual properties. Rare earth oxide is a good heat radiation material, and it seems that metallic surfaces coated with rare earth oxide radiate heat much faster than do untreated surfaces.

RARE EARTHS IN PLASTICS. We frankly don't know what sort of things rare earth-impregnated plastics could be used for, but a couple of people have taken enough interest in this problem to make up experimental samples. We've been doing some playing with them ourselves and have some ideas about using them. Polyethylene, for example, can be fabricated to hold up to 5 to 10 times its weight of rare earth oxide, and we've even seen some precision-bore epoxy tubing made with a rare earth oxide filler.

SEPARATION AND SAMARIUM. We are like a slaughter house in that we would like to use everything that a rare earth separation process turns out, including the squeal. With the interest that has been generated in using gadolinium as a neutron absorber (thermal cross section about 46,000 barns), we have accumulated quite a pile of samarium oxide in rather decent purity. In the process of separating gadolinium and some of the other rare earths, samarium is produced as a by-product. If you can think of a use for samarium, we have the samarium compounds.

RARE EARTH GARNETS. These are structurally somewhat similar to the garnet variety grossularite (formula $Ca_3Al_2(SiO_4)_3$). The most interesting ones are the rare earth-iron garnets such as $Y_3Fe_2(FeO_4)_3$. This mouthful of formula has been abbreviated by researchers to "YIG" for obvious reasons. Other names stem from other rare-earth symbols. These garnets, particularly those of yttrium, gadolinium, erbium, and some others have interesting ferromagnetic properties, making them useful as ferrite materials in electronic equipment. We don't make the garnets, but we do make the rare earth oxides needed to prepare them.

SINTERED SHAPES. One of our friends once wanted to know if rare earth oxides could be pressed and sintered into shaped pieces. Apparently they can, and our friend made up some experimental hot-pressed rare earth oxide and cerium oxide pieces for us.

Lindsay produces thorium and rare earth salts in purities up to 99.99% for a rather surprising variety of chemical and industrial applications. Most of these materials are available for prompt shipment in quantities from a gram to a carload.

We will be pleased to supply your research and process development people with technical data, analyses, prices and whatever may be helpful to you in exploring the possibility of the profitable application of rare earths to your own problems.

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The Long Pull

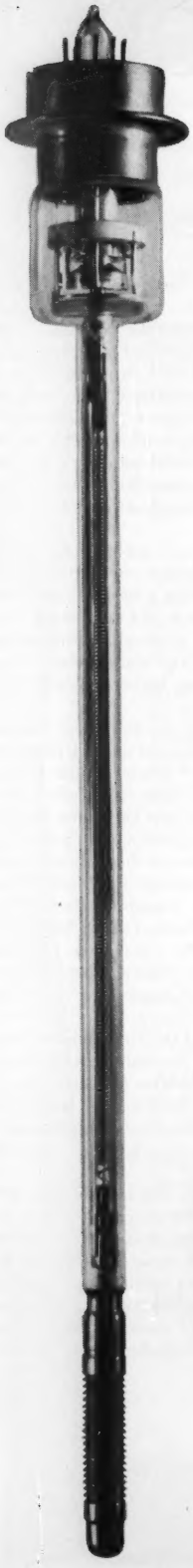
The launching of the sputniks in October and November brought to a much wider public the realization that the Soviet Union has attained a high level of scientific and engineering competence. Neither the existence of this competence nor the methods by which it has been attained is news to those American scientists who have visited the Soviet Union in recent years or to those who have followed the Soviet scientific literature. The methods are simple and straightforward: education in the sciences and mathematics in the schools and universities is intense and prolonged; all who show talent in the sciences have an opportunity to go into more advanced work; those who attain professional standing are handsomely rewarded both in material benefits and status in the community; research, both basic and applied, is strongly supported.

The challenge to this country cannot be met, except perhaps on a short-term basis, by crash programs in particular enterprises or by shifting scientists and engineers from one project to another. What is needed to prevent us from slipping into a secondary position in science and technology over the long pull of the next ten to twenty years is a thorough reform of our educational system from grade school through college and a means of assuring that talented students are not barred from higher education for reasons of race, religion, or financial resources.

Reform, if it is to come, will require, among other things, radical changes in the public attitude toward intellectual accomplishment and a willingness to provide adequate pay and status for teachers. Certainly, such reform should be our long-term goal, but a more immediate gain can be effected by making an effort to remove the financial barrier that now bars some 100,000 well-qualified high school graduates from further education each year. The costs of education have been steadily rising, and some of the increased costs have been passed on to students even in the state universities. Many of the state universities were originally tuition-free on the assumption that society was the beneficiary of education and that a democratic society should not put financial barriers in the way of its economically less favored families. The trend away from free tuition is based on the premise that students benefit from higher education and that they will appreciate education more if they pay for it.

The President's Committee on Education Beyond the High School (Second Report to the President) has, in the main, favored the last set of assumptions. It recommends that the needs of students for financial support be met by private, local, and state scholarships, by federally supported "work-study" programs, by credits on income tax for educational expenditures, and by the provision of privately financed loans at low rates of interest to students or parents.

All of these measures are good as far as they go, but is the committee wise in rejecting for the present a Federal scholarship program? The committee notes the recent expansion of scholarship support by industry, labor unions, and state and local governments. It adds, "If these programs should later prove to be inadequate, the Committee believes a Federal scholarship program to fill the gap is inevitable." But recent events have put a premium on time. Can we afford to lose tens of thousands of talented people from higher education each year while we wait to see whether or not private sources can foot the bill?—G. DUS.



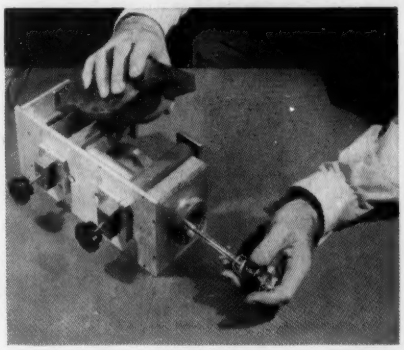
A GREAT AMPLIFIER TUBE IS PERFECTED FOR TELEPHONY

A new transcontinental microwave system capable of carrying four times as much information as any previous microwave system is under development at Bell Laboratories. A master key to this development is a new traveling-wave tube of large frequency bandwidth.

The traveling-wave amplifying principle was discovered in England by Dr. Rudolf Kompfner, who is now at Bell Laboratories; the fundamental theory was largely developed by Labs scientist Dr. John Pierce. Subsequently the tube has been utilized in various ways both here and abroad. At the Laboratories it has been perfected to meet the exacting performance standards of long distance telephony. And now for the first time a traveling-wave tube will go into large-scale production for use in our nation's telephone systems.

The new amplifier's tremendous bandwidth greatly simplifies the practical problem of operating and maintaining microwave communications. For example, in the proposed transcontinental system, as many as 16 different one-way radio channels will be used to transmit a capacity load of more than 11,000 conversations or 12 television programs and 2500 conversations. Formerly it would have been necessary to tune several amplifier tubes to match each channel. In contrast, a single traveling-wave tube can supply all the amplification needed for a channel. Tubes can be interchanged with only very minor adjustments.

The new amplifier is another example of how Bell Laboratories research creates new devices and new systems for telephony.



Left: A traveling-wave tube. *Right:* Tube being placed in position between the permanent magnets which focus the electron beam. The tube supplies uniform and distortionless amplification of FM signals over a 500 Mc band. It will be used to deliver an output of five watts.

BELL TELEPHONE LABORATORIES

WORLD CENTER OF COMMUNICATIONS RESEARCH AND DEVELOPMENT

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Lake Agassiz and the Mankato-Valders Problem

John A. Elson

Recent papers by Wright (*1*), Wright and Rubin (*2*), and Leighton and Wright (*3*) have dealt with the problem of correlation of Port Huron, Valders, and Mankato drift. Leighton suggested that the term *Mankato* be applied to a substage between Cary and Valders drift and suggested the Bigstone moraine as the western equivalent, in Minnesota and the Dakotas, to Valders.

Work of the Geological Survey of Canada (*4*), now being prepared for publication, yielded carbon-14 material dated at Yale early in 1953 that established the Two Creeks age of the Lake Agassiz I–II interval. The dates imply (i) that the Valders ice advanced little farther southwest than The Pas moraine in Manitoba and not as far southwest as Fort Frances in western Ontario, and (ii) that the Lake Agassiz basin drained eastward into the Lake Superior basin in Two Creeks time. In a search for eastern outlets of Lake Agassiz, air photographs of the area north and west of Lake Superior were examined, with satisfying results, although correlations of the moraines and outlets discovered await field studies. This article is a brief review of data on Lake Agassiz in the light of radiocarbon dates; it shows that the Valders ice border probably lay well inside the margin of the Canadian Shield in western Ontario and northern Manitoba and that the Cary-Mankato retreat and readvance were minor compared with the Mankato-Valders marginal fluctuation.

Early Lake Deposits

The oldest carbon-14 date obtained on deposits underlying Lake Agassiz is from Bronson, Minnesota (samples W-102 and W-468, $>36{,}000$ years). This pre-Wisconsin deposit may correlate with 12 or 14 other interglacial occurrences, some containing organic matter and some not, that apparently underlie the same till sheet in and near the Lake Agassiz basin (*5*). No breaks in the overlying till sheets that can be attributed to subaerial erosion are known, although a striated boulder pavement is widespread in southern Manitoba (*6*); it may be the subglacial expression of a marginal retreat and advance of substage magnitude. Most, if not all, of the Lake Agassiz basin and probably all of western Ontario and Manitoba were covered by ice throughout Wisconsin time prior to the retreat from the Mankato-Port Huron moraine system.

Lake Agassiz I

Mankato till is overlain by the clays of Lake Agassiz I except where thin, lenticular deposits of sand and gravel, presumably deposited at the base of the ice margin standing in Lake Agassiz rather than subaerially, occur between them. Minor glacial readvances represented by till in and overlying sediments of Agassiz I are not known south of Lake of the Woods and Fort Frances (*7*).

Lake Agassiz II

Overlying the clays of Lake Agassiz I, unconformably, are the silty deposits of Lake Agassiz II. The disconformity, which may be recognized by the character of Agassiz II sediments—which are locally sandy and commonly contain gastropod shells and organic matter near the base (*5, 8, 9*)—by valleys eroded in the older sediments (*5, 6, 8*), and by drying surfaces recognized by soil mechanics tests (*10*), has been reported from about 25 localities. Till has been reported overlying clays of Lake Agassiz near Sioux Lookout (*11*), at Steep Rock Lake (*12*) in Ontario, and near Steinbach and Rosa in southeastern Manitoba (*13*), but correlation of the stratigraphy is not established, and the sediments may be Agassiz I. At the north end of Lake Winnipeg (*5*, pp. 145–146), 12 miles north of The Pas moraine, till overlies sediments characteristic of Lake Agassiz II.

Extensive areas of the lake floor have no lacustrine clay or silt, partly because of removal by wave action during subsidence of the lake and partly because no major river contributed sediments to those parts of the basin. Rivers seem to have contributed most of the sediments to Agassiz II, whereas glacial contributions were confined to a belt near the ice margin. The ice margin retreated across Agassiz I, so both glacier and rivers contributed to its deposits.

When the Lake Traverse outlet of Lake Agassiz I eroded down to bedrock, the water stood at a constant level and formed the Campbell strandline, generally a distinctive scarp with a massive beach at its toe that can be traced for hundreds of miles; it extends north of latitude 53° on the west side of the lake basin. A second, slightly lower Campbell strandline formed after the Agassiz I–II subaerial interval, when advancing Valders ice and possibly crustal uplift north of Lake Superior blocked the eastern drainage of the basin and formed Lake Agassiz II, which discharged southward through the Lake Traverse outlet for part of its history.

The Agassiz I–II interval has been dated by a radiocarbon sample from the base of Agassiz II sediments at Moorhead, Minnesota, at 9930 ± 280 years (W-388). Five dates on samples obtained in the Assiniboine Valley span part of the Agassiz I–II interval and the rising phase of Agassiz II: Y-165, sandy peat ($12{,}400 \pm 420$ years); Y-166, shell ($11{,}230 \pm 480$ years); and three recently published dates, Y-411, wood ($10{,}550 \pm 200$ years); Y-415, wood (9110 ± 110 years); and Y-416, peat (8020 ± 100 years) (*14*), from successively higher

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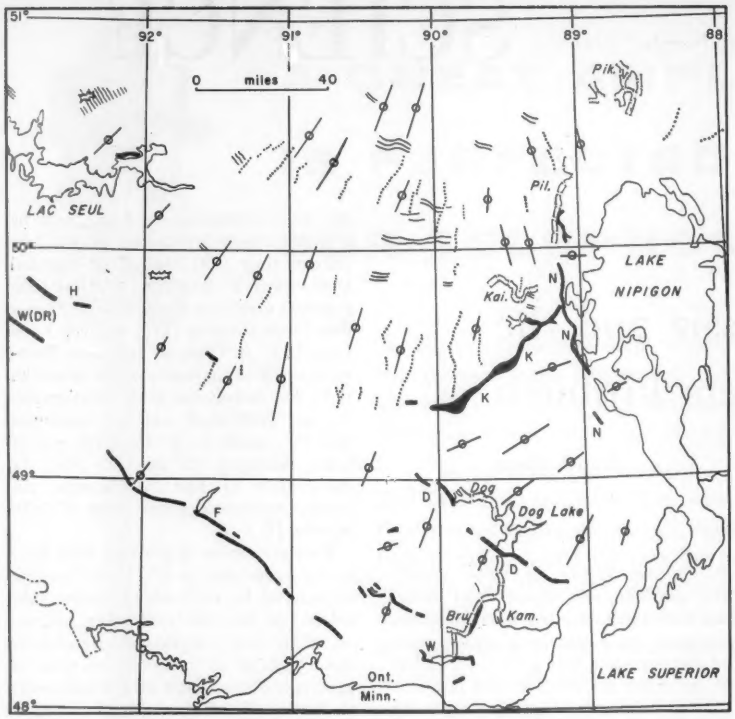

Fig. 1. Sketch map of area containing the eastern outlets of Lake Agassiz, showing glacial features interpreted from air photographs. End and interlobate moraines are black, with vertical letters: *D*, Dog Lake moraine; *F*, Finlayson; *H*, Hartman; *K*, Kaiashk (interlobate); *N*, Nipigon; *W*, Whitewater; *W(DR)*, Wabigoon (Dryden). Spillways are bracketed, with slanted letters: *Bru.*, Brule Creek; *Dog*, Dog River; *Kai.*, Kaiashk River; *Kam.*, Kaministikwia River; *Pik.*, Pikitigushi River; *Pil.*, Pillar Lake. The trends of washboard moraines are shown as thin parallel lines. The principal eskers are dotted. The trend of glacially streamlined features is shown by straight lines and circles. Areas of wave-cut terraces have cuspate outlines.

positions in an alluvial fill. The six dates span the Two Creeks interval. Because the Campbell strandline extends north of latitude 53° and apparently has not been overriden by ice, the Valders glacier obviously could not have extended south of that latitude on the west side of Lake Agassiz. Its margin probably stood at The Pas moraine.

Boundaries to the East

Locating the ice border in the eastern part of the lake basin is much more difficult, because both ice advance and crustal uplift may have participated in closing the eastern outlets and because features associated with ice advances and lake outlets are not necessarily obvious in the air photographs of the wild, rugged, forested country of western Northern Ontario. Figure 1 shows moraines and outlets discovered in a reconnaissance study of 1-inch-to-1-mile photographs at the National Air Photo Library in Ottawa.

Portions of the Dryden-Wabigoon-Finlayson (Steep Rock Lake)-Whitewater moraine system have been described in the literature (*12, 15*); east of Whitewater Lake this moraine curves south as if to join the Highland or the Fond du Lac moraine in Minnesota. This moraine seems to represent a glacial advance east of Lake Agassiz during intermittent retreat in the western part of the basin.

The Dog Lake moraine, apparently not reported hitherto, is a splendid example of an end moraine with outwash fans, and it obstructs, in two places, the spillway formed by Dog River and Kaministikwia River. Including gaps, the moraine can be traced for at least 58 miles, from latitude 49°N, longitude 90°W southeast to the wave-washed, bare rock area 5 miles north of Thunder Bay on Lake Superior. It may correlate with the Kaiashk interlobate moraine, another well-defined feature that extends 50 miles southwest from the west side of Lake Nipigon, or it may represent the landward end of a slowly retreating ice margin that stood in Lake Agassiz and extended west and north to the Sachigo moraine. It is a possible candidate for designation as a Valders end moraine.

A third end moraine trends south along the west side of Lake Nipigon (*16*); the ice that formed it may have blocked the Kaiashk River outlet of Lake Agassiz. North of its intersection with the Kaiashk interlobate moraine the Nipigon moraine forms a sharp boundary between features indicating south-flowing ice to the west and west-flowing ice to the east. An eastward shift of a center of outflow is suggested. Almost as good a case can be made for correlation of the Nipigon moraine with Valders as for the Dog Lake moraine. Further comment on the correlation of these moraines would be mere speculation.

Broad, flat-floored spillways, either dry or containing underfit streams, form parts of the drainage systems of Kaministikwia, Dog, Kaiashk, and Pikitigushi rivers (Fig. 1). All of these may have functioned as eastern outlets of Lake Agassiz at different times.

Previously unreported terraces, interpreted as having been wave-cut during submergence in Lake Agassiz, occur on drift hills south of Minnitaki Lake and north of Lac Seul. Similar wave-cut benches occur on the Sachigo interlobate moraine south of Sachigo Lake (latitude 53°35′N, longitude 92°25′W). Altitude determinations of these features will be of assistance in the search for the eastern and northern boundaries and outlets of Lake Agassiz II. Late in its history the lake may have discharged northward, east of the Sachigo moraine, by way of Echoing River spillway into Hudson Bay, prior to marine submergence of that area.

Valders Ice Border

Probably the Valders ice border extended from the type area in Wisconsin northward, past the west side of Lake Nipigon, north-northwest to Sachigo Lake, west to The Pas moraine, which is almost certainly of Valders age, and northwest to the Cree Lake moraine in northern Saskatchewan. This border (Fig. 2) is compatible with the minimum retreat of the ice in Two Creeks time shown by R. C. Murray (*17*). A lesser retreat and readvance, between Cary and Port Huron-Mankato time, would account for the red drift of the Superior Lobe (*18*), the Dryden-Finlayson Whitewater moraine, and the till over varved clay near Sioux Lookout (*11*) and at Steep Rock Lake (*12*).

If the Coteau de Missouri represents the outer limit of the Mankato ice on the prairies, the minimum average width of ice removed in Manitoba and Sas-

katchewan in Mankato-Valders time is about 400 miles. Mankato drift may extend west of the Coteau (Fig. 2). The ice margin withdrew northwestward and later northward, breaking up into sublobes as it moved (*6, 19*); hence, the marginal retreat from the Mankato end moraine of the Des Moines lobe was at least 750 miles west of longitude 96°, and about 250 miles nearer Lake Superior.

The amount of advance of the Valders ice sheet in the west is not known, but it was probably much less in northern Saskatchewan than in Michigan and Wisconsin, because of slower metabolism of the ice sheet, due to low temperatures and precipitation. The retreat alone suggests a more significant climatic fluctuation than that so far demonstrated for the Cary-Mankato interval. I feel that the term *Mankato* is useful to denote drift referable to the Mankato-Port Huron moraine system but that it is more closely related to Cary than to Valders. Whether or not a drift sheet whose known margin lies mainly within the United States deserves substage rank is not for a Canadian to decide.

History of Glacial Lake Agassiz

A working hypothesis of the sequence of events in the history of Lake Agassiz follows; a summary of all the evidence would be too lengthy for presentation here.

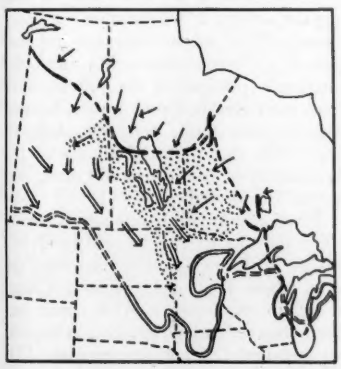

Fig. 2. South-central Canada and adjacent United States, showing known and postulated positions of Mankato-Port Huron (double line) and Valders (single heavy line) drift borders. Lines are solid where drift borders are known, or along end moraines, and are broken where drift borders are interpolated or postulated. Arrows indicate directions of ice flow; double arrows are Mankato, single arrows are very late Mankato and Valders. Lake Agassiz II is stippled. Directions are based in part on studies of air photographs taken in Saskatchewan, Manitoba, and northern Ontario and on field studies made in southern Manitoba and Saskatchewan.

1) Prior to lake formation there occurred a pre-Wisconsin interglacial interval.

2) An early proglacial lake was overridden by the advancing Wisconsin glacier.

3) An interval of glacial nondeposition or subglacial erosion formed a striated boulder pavement, probably during a late-Wisconsin interstadial.

4) A minor re-expansion of the ice sheet was followed by deposition of the Mankato (Altamont)-Port Huron moraine.

5) Intermittent northward retreat of Mankato ice resulted in the formation of Lake Agassiz I, which discharged southward through the Lake Traverse outlet (River Warren). The Sheyenne, Elk Valley, Pembina, and Assiniboine deltas, with corresponding moraines, were deposited in Lake Agassiz against the ice margin. There was contemporaneous retreat in the Lake Superior basin (Lake Keweenaw?).

6) The southern Agassiz outlet was eroded down to the Tintah or Norcross level, when retreat of the glacier in the Lake Superior basin opened an eastern outlet (Brule Creek?). The ice margin in the west retreated slightly north of Duck Mountain (latitude 53°N).

7) A minor readvance in the west deposited the Cowan moraine on Duck Mountain; a major advance in the east filled Superior basin and deposited red drift in northeastern Minnesota; the ice margin stood at the Dryden-Finlayson-Whitewater moraine.

8) Lake Agassiz I eroded its southern outlet down to a bedrock sill; the higher Campbell strandline was formed; the ice margin began to retreat; the Campbell strandline was abandoned when retreat again opened eastern outlet(s) (Dog River and others farther north).

9) The Lake Agassiz I–II interval (Two Creeks) followed. Withdrawal of ice into northern Ontario prior to major crustal upwarping opened lower outlets, and the Agassiz basin was drained. Erosion of lake floor and delta sediments occurred, and a molluscan fauna invaded the region. Prairie floras spread eastward across the dry lake basin. The Little Minnesota River deposited an alluvial fan at Browns Valley in the abandoned southern outlet.

10) Advancing ice (Valders) formed Lake Agassiz II. The eastern outlets were blocked by the advancing ice sheet and possibly also by crustal uplift. The ice margin extended from west of Lake Nipigon north to Sachigo moraine, west to The Pas moraine, and northwest to Cree Lake moraine. Lake Agassiz II discharged eastward until its highest available outlet (Dog River?) was blocked (Dog Lake moraine?), then rose and overflowed the alluvial fan damming the southern outlet at Browns Valley; the lake level temporarily rose to the former Norcross or Tintah stand, and alluvial fills were deposited in the Pembina and Assiniboine valleys. Then the Browns Valley alluvial dam was swept away, and the lake rapidly subsided to the second Campbell strandline, which is slightly lower than the first because of erosion of the outlet and crustal upwarping. Plainview and Agate Basin (lanceolate) projectile points were distributed around Lake Agassiz II.

11) The retreat of Valders ice opened eastern outlets north of the moraine-dammed and uplifted Dog River spillway; the Kaiashk and Pillar Lake outlets successively discharged southward into Lake Superior through Black Sturgeon spillway. Subsequently Pikitigushi and other northern spillways conducted Lake Agassiz discharge to Lake Superior by way of Lake Nipigon. The Campbell strandline was abandoned, and others formed at successively lower levels.

12) A northern outlet opened east of the Sachigo interlobate moraine when residual ice in Keewatin District (*20*) was severed from retreating Laurentide ice by melting into incipient Hudson Bay. Discharge through this outlet occurred prior to marine submergence and subsequent crustal uplift.

13) Residual ice in the Nelson River basin melted, and Lake Agassiz drained northward into Hudson Bay, prior to 3600 years ago, at which time Lake Shore projectile points (Signal Butte IA) were distributed throughout the basin. Forest flora invaded the eastern part of the basin, surrounding small prairie refuges that had formerly been on islands and on the eastern shore of Lake Agassiz II (*21, 22*).

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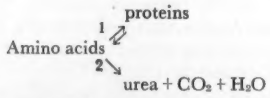
22. *Erratum ad referendum.* This is a suitable place to correct an error that has recurred in a generation of reference books [the most recent examples are J. K. Charlesworth, *The Quaternary Era* (Arnold, London, 1957), p. 476, and W. D. Thornbury, *Principles of Geomorphology* (Wiley, New York, 1954), p. 408]. Although a glacial lake in the lower Saskatchewan Valley may have merged with Lake Agassiz, glacial lakes Regina and Souris were entirely separate lakes. Neither merged with the other, and neither merged with Lake Agassiz.

Endocrine Control of Amino Acid Transfer

Distribution of an Unmetabolizable Amino Acid

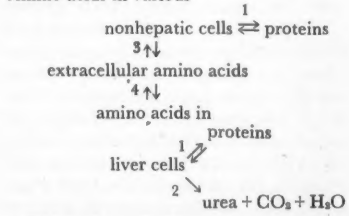
Matthew W. Noall, Thomas R. Riggs,
Lois M. Walker, Halvor N. Christensen

We can greatly oversimplify a description of amino acid metabolism by writing



The remarkable features which dominate amino acid metabolism in the higher animal are (i) the large shift from fate 1 (anabolic) to fate 2 (catabolic) which takes place when the animal passes from fetal life and infancy to adulthood and (ii) the large shifts which can be induced experimentally, either by administering a hormone or by producing conditions which stimulate secretion of hormones.

The hypophyseal growth hormone and certain androgenic steroids are recognized to have strong anabolic effects, and some of the adrenal cortical steroids, strong catabolic effects. In addition, other hormones, notably the estrogens, produce growth of particular tissues. Before trying to explain these effects, we must complicate the above scheme by remembering that anabolism and catabolism do not take place from a single homogeneous pool. We can write instead, as a second approximation



This scheme reflects the conclusion that most of the *net* degradation of amino acids occurs in the liver, whereas only hepatic proteins and some of the circulatory proteins are formed in the liver.

Steps 3 and 4 are *concentrative transfers* of the amino acids into the cells—that is, transport against concentration gradients, discovered in 1913 by Van Slyke and Meyer (*1*). The process has been extensively studied (*2, 3*), and may well be a restrained form of similar activities found in lower forms of life, which, however, have not yet been shown to be definitely concentrative.

Accordingly, concentrative transfer undoubtedly was developed before hormonal control; hormonal *restraint* appears, instead, to have been superimposed upon a primitive activity. In some microorganisms concentrative transfer may be substrate-induced (*4*). Concentrative transfer occurs across many cell barriers, such as the placental barrier (*5*), the renal tubular cells, and the intestinal mucosa, but also occurs across the cell barrier of most other cells so far studied (see Gale, *6*). It is a common step through which every amino acid must pass before it can be utilized. We have delayed calling the activity a "transportase" or "concentrase" (or, as one colleague has suggested, a "here-to-there-ase") until the enzymatic portions of the process have been more clearly demonstrated. A more objectionable term, *permease*, suggests incorrectly that we are dealing with the breakdown of barriers to diffusion, and should be rejected.

Paradoxically, we have observed many times that the free amino acid levels are higher in the more rapidly growing tissues, where they ought instead, if anything, to be depleted. This result has been observed in fetal life (*5*), in hepatic regeneration (*7*) and in neoplasia (*8*). Might an estrogen, for example, stimulate growth of the uterus, by increasing the extent to which that tissue concentrates amino acids? Might growth hormone increase the extent to which various tissues capture amino acids? Might the catabolic steroids increase particularly the hepatic capture of amino acids, thereby exposing them to accelerated destruction?

Such questions were asked (*9*), and the latter one tentatively answered in the affirmative, in 1948 (*7*), when hepatic amino acid levels were found to be increased in the rat after laparotomy. In

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the human patient, plasma amino acids are lowered by trauma or surgery or febrile illness; this effect might also arise from increased hepatic uptake.

Procedure and Analysis

Unequivocal demonstration of the regulation of amino acid metabolism at this common transport step has not been possible heretofore, although many observations have been in agreement with such regulation. The difficulty has been to distinguish possible effects upon anabolic and catabolic reactions themselves from effects upon transport. This has now been accomplished by the use of an unmetabolizable amino acid, α-aminoisobutyric acid (AIB), which undergoes concentrative transfer in an apparently normal fashion, being strongly concentrated by cells, and therefore only slowly excreted from the animal. The synthesis is described elsewhere (*10*).

The earlier observations of nonmetabolizability made at high dosage levels (*11*) were confirmed at tracer doses. At 1 milligram per kilogram of body weight, not over 0.02 per cent of the radioactivity was excreted as CO_2, nor could radioactivity be detected in tissue proteins.

Furthermore, AIB was excreted in the urine entirely in its unchanged form. Only one radioactive spot was detected on paper chromatograms [$R_f = 0.64$ in *n*-propanol–0.1*N* aqueous ammonia (1/1) and 0.83 in *n*-butanol–water–acetic acid (5/5/1), the amino acid fed giving the same R_f values]. Under these conditions even 1 percent of the dose excreted in another form might have been detected. Fecal excretion was very low. Appreciable levels of the amino acid were found present in the rat after 3 days, showing that a generous period was available for study of endocrine effects upon its distribution. We have waited either 20 hours (estradiol), 30 hours (epinephrine and growth-hormone) or 39 hours (all other experiments) after injection of AIB before observing its distribution. In all cases the animals were fasted about 15 hours before they were sacrificed.

For analysis, tissues were homogenized with 5 parts of very dilute acetic acid (to give a *p*H of about 5), and the extracts were heated to deproteinize them. Serum and urine were counted directly. A thin-windowed gas-flow counter was used throughout, correcting for self-absorption.

Effect of age or body weight on the distribution of the amino acid. Figure 1 shows that progressively higher serum levels resulted from the standard dose as the rat grew larger. This rising serum level was mainly caused by the declining activity of the tissues in concentrating the amino acid from the extracellular fluid, which is illustrated in Figure 2 for the skeletal muscle. The ordinate shows the "distribution ratio"—that is, the number of times that the amino acid appeared to have been concentrated by the cells; levels for the cellular and extracellular water were calculated by using available figures for the fluid compartment relationships.

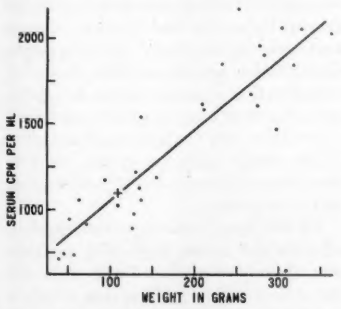

Fig. 1. Rising serum levels reached after administration of a standard dose of AIB, with increasing body size. One milligram of AIB per kilogram of body weight was injected 39 hours before analysis. The correlation coefficient is 0.883.

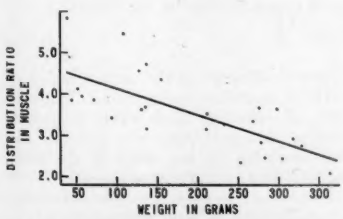

Fig. 2. Decreasing "amino acid hunger" of a tissue with increasing size of the rat. Same animals as in Fig. 1. The distribution ratio is the ratio of the tissue level of AIB to the serum level, both expressed in counts per kilogram of water. The correlation coefficient for the line is −0.696.

The same result was obtained for a number of other tissues. The younger tissues showed a stronger "amino acid hunger," and the plasma level was thereby lowered; the older tissues lived in a richer medium and yet captured relatively less of the amino acid. This metabolically useless amino acid reflects the decreasing "amino acid hunger" because it corresponds structurally to the rather modest requirements for transport.

Adulthood is not as distinct an entity in the rodent as it is in man; it will be interesting to see whether this change in avidity of tissues for amino acids occurs more abruptly at maturity in the human.

Effect of epinephrine. Epinephrine has long been known to depress the level of the plasma amino acids, although in an unknown way. Figure 3 demonstrates that almost all tissues had increased levels of AIB 2 hours after 0.1 milligram of epinephrine per kilogram of body weight had been injected. With 12 animals (adrenalectomized females, 180 to 220 grams) in each group, the changes were statistically significant ($P < 0.02$) in the case of heart and kidney. The amino acid had been injected 30 hours earlier.

Pituitary growth hormone. Intramuscular injection of 1 unit of pituitary growth hormone in 200-gram female rats likewise intensified in 2 hours the concentration of AIB for all tissues studied except the heart (Fig. 4). Each group included nine animals. The changes for the liver, kidneys, duodenum, and the combined ovaries plus uterus were highly significant by statistical test.

Influence of hydrocortisone. The action of adrenal steroids was first discovered as an indirect effect of vitamin B_6-deficiency. This deficiency decreased the intensity with which various tissues concentrated AIB (*12*), supporting the role of pyridoxal in amino acid transport. The liver was a prominent exception, however, capturing if anything more AIB than usual in the deficiency; but when the animals first had been adrenalectomized, the behavior of the liver was no longer disparate.

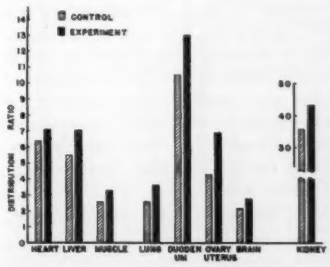

Fig. 3. Effect of epinephrine on the accumulation of AIB by adrenalectomized rats. The dose was 0.1 milligram per kilogram of body weight. Other values are averages for 12 animals.

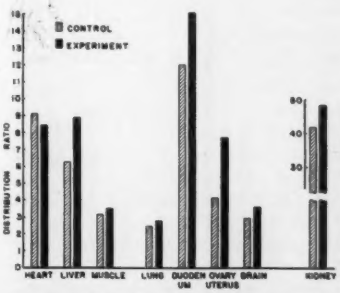

Fig. 4. Effect of growth hormone on the accumulation of AIB by rats. The dose was 1 unit per animal of body weight about 200 grams.

Figure 5 shows the normal relationship between serum AIB and liver AIB levels. The latter remained 8 or 9 times the concentration of the former. This is the kind of relationship that was found for glycine in the intact guinea pig in 1948 (*13*) and that has since been shown repeatedly with isolated cells and tissues.

Table 1 shows the disturbance in this relationship with the hepatic AIB capture increased by about 60 percent 2 hours after injection of 2 milligrams of hydrocortisone subcutaneously into the 135-g rat. The test amino acid (1 mg/kg) had been injected 39 hours earlier. This response in 2 hours is more rapid than the effect obtained by Engel upon urea formation (*14*). The prompt and vigorous action cannot be attributed to acceleration of amino acid catabolism: there *was no catabolism* of the model amino acid.

A question often discussed is whether the catabolic phase following surgery or trauma ought, if possible, to be eliminated or whether it serves a protective purpose, perhaps by flooding the injured site with building stones for repair. Such an effect is not to be expected, however, if catabolism is induced by intensified hepatic capture of amino acids. The tissue wastage appears to be initiated by a *pull* rather than a push, and therefore the catabolic phase probably does not flood the injured site with repair materials. A relatively slight intensification of the concentration of AIB by nonhepatic tissues was possibly also produced by hydrocortisone; but with a metabolizable amino acid this could scarcely compensate for the intensified destruction of the amino acid.

Referring again to the second scheme, we see that the liver not only destroys amino acids but also synthesizes them into a number of proteins. Interestingly, hydrocortisone accelerates the synthesis of plasma albumin (*15*) and of a number of liver proteins. Such an acceleration might be anticipated under the present thesis of the mode of steroid action. Hepatic gluconeogenesis from amino acids should also be stimulated. Furthermore, the retarding influence of administered sugar on amino acid catabolism (*16*) is readily understood.

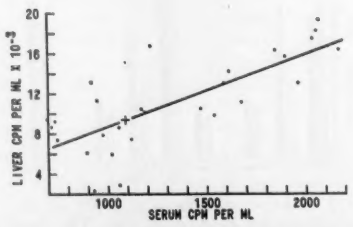

Fig. 5. Relationship between the serum and liver concentration of AIB in normal rats. The correlation coefficient is 0.744.

Table 1. Effect of administering hydrocortisone on AIB distribution. All values are thousands of counts per minute, per milliliter, followed by the standard error. The only statistically significant change is the intensification of the liver concentration. Although the hepatic levels could be seen by inspection to be clearly elevated, the following conservative method of calculation was used: The control levels for rats of the body weight taken (137 grams, standard deviation 13.5 grams) were obtained from regression lines versus body weight based upon 29 normal animals. The serum levels of the eight experimental animals averaged 1440 counts per minute, per milliliter; therefore one can predict the tissue values in the second column, based upon regression lines like those of Fig. 5.

Tissue	Normal distribution for a 137-g rat	Normal distribution for a 137-g rat, adjusted to a serum level of 1440 count/min ml	Found 2 hr after administration of hydrocortisone
Serum	1.21 ± 0.04	1.44	1.44 ± 0.10
Muscle	4.73 ± 0.31	5.78 ± 0.63	5.72 ± 0.29
Liver	10.17 ± 0.57	11.06 ± 1.71	17.50 ± 0.93
Kidney	45.4 ± 2.2	55.7 ± 4.7	64.2 ± 4.8
Heart	8.62 ± 0.66	9.87 ± 0.99	10.6 ± 0.39
Duodenum	18.9 ± 0.7	20.72 ± 1.45	18.54 ± 0.23

Estradiol. Four 21-day-old female rats were injected intraperitoneally with the tracer dose of AIB and subcutaneously with 0.1 microgram of estradiol in 0.1 milliliter of sesame oil. Four control animals received, instead, AIB and pure sesame oil. After 20 hours the animals were sacrificed, and samples of plasma, uterus, and liver were analyzed (Table 2). At the time of sacrifice the uterus had entered a phase of rapid growth under the influence of the estrogen (*17*). For the liver, no intensification of AIB concentration was observed, but now the uterus concentrated the amino acid by 280 percent of the original value.

Discussion

Several endocrine agents of widely different character are thus seen to influence the ability of cells to capture amino acids from the surrounding medium, in directions consistent with their growth-promoting and catabolic actions. The changes observed with AIB are consistent with many of the observations already made of hormone action on the distribution of the ordinary amino acids, indicating that this amino acid responds like other amino acids to humoral influence. The following effects, for example, have been shown: (i) decreased plasma amino acids accompanied by increased total free amino acids in the dog receiving growth hormone (*18*); (ii) decreased plasma amino acids after stress in man, increased liver amino acids after surgery in rats (*7*), and decreased plasma amino acids in rats receiving hydrocortisone (*19*); and (iii) decreased plasma amino acids after epinephrine injection.

For all of these changes there has always remained the possibility that the influences were at other points than the transfer step; but for AIB, possibilities other than the transfer reaction appear to be eliminated.

Probably we should be oversimplifying matters were we to imply that all cellular reactions which use amino acids are necessarily accelerated when a cell concentrates amino acids more strongly. Quantitative aspects, such as the extent and duration of action, must be considered. Furthermore, increased capture at a given site may be deprived of net effect if the amino acids are drawn away by simultaneously increased hepatic capture and destruction.

Finally there is the important question whether the amino acid-using reactions may already be saturated with respect to the various amino acids, so that no stimulation would result from elevated levels. Clearly, this is not the case for catabolic breakdown in the liver; we all know how readily this rate adjusts itself to the level of protein intake; therefore one may confidently expect accelerated amino acid breakdown to follow intensified amino acid concentration by the liver.

Table 2. Change in the accumulation of AIB by immature uterus upon administration of estrogen. Each value represents results obtained from one animal. The concentration by the livers of the same animals was not detectably altered.

Distribution ratio, uterus/serum	
Control	Experimental
5.55	16.6
4.23	13.6
5.01	14.7
4.83	9.62
Mean 4.90	Mean 13.6

For reactions of protein synthesis, the question has not been answered as completely. Broad ranges have been observed over which the rates of incorporation of an amino acid or of the net synthesis of protein *in vitro* do vary with the amino acid level; but such ranges are not yet adequately defined for the various tissues *in situ*. In addition, mutual supplementation experiments among the amino acids have shown how readily one amino acid may fall to levels suboptimal for growth.

Furthermore, the finding should be considered that amino acid levels are rather uniformly high where protein synthesis or growth is accelerated. Before we can imply a causal relationship in this association, we must consider one alternative explanation. Protein synthesis undoubtedly proceeds through activated amino acid intermediates; by spontaneous dissociation, these intermediates (or the proteins themselves) might release amino acids at high levels. At high synthetic rates such intermediates might be more abundant, and the free amino acids could therefore reach higher levels. (Such a hypothesis must also assume that the precursor amino acids are taken from one compartment—for example, the cell exterior—and that the intermediates are dissociated into another—for example, the cell interior). For example, when the immature uterus entered an estrogen-stimulated growth phase, perhaps the high amino acid levels were a secondary expression of the high rate of protein synthesis.

Such an explanation becomes highly improbable, however, for the present observations. α-Aminoisobutyric acid is not incorporated into protein, and it is unlikely that it proceeds even to intermediate stages of that synthesis. For example, no stimulation by it of the exchange of radioactive phosphorus between pyrophosphate and adenosine triphosphate has been detected (*20*). Accordingly, the reaction which was stimulated upon administration of estrogen was most likely the transfer reaction itself.

Note that estradiol intensifies AIB concentration by the uterus and not by the liver, whereas hydrocortisone intensifies mainly the hepatic capture. If we assume that the same amino acid carrier operates in these two tissues, there must be local factors which make the transport more susceptible to an endocrine agent in one tissue than in the other. For example, a particular hormone molecule might gain access to the transport apparatus more readily in one than in the other.

Apparently we have in nitrogen metabolism additional instances of endocrine control operating on transfer reactions. Certain other steroids are already recognized to influence the transfer of Na^+ and K^+ between cells and surrounding fluids, and insulin has been shown to increase the access of sugars to the cell interior (*21*). The fate of the amino acids appears to be collectively modified by changing the extent to which various cells concentrate amino acids from the extracellular environment.

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22. The experimental work described in this article was supported in part by a grant (C-2645) from the National Cancer Institute, U.S. Public Health Service. One of us (M. W. N.) held a fellowship of the American Cancer Society during the major part of this work.

Ward Vinton Evans, Physical Chemist

On 2 August 1957, Ward Vinton Evans died in Rawlinsville, Pennsylvania, where he had been born 77 years before.

His professional activities had made him well known within his own scientific group, but his part on the world stage did not come until 1954 when, well into his 70's, he served on the special three-man security board which reviewed charges against J. R. Oppenheimer. Before this, he had served on a number of review boards dealing with security clearances in the Chicago area. His dissent from the majority finding against Oppenheimer attracted world-wide attention. As the *Washington Post* said in an editorial on his death, "his pungent dissent from the majority finding against Dr. Oppenheimer, written in earthy language, stands as a model of clarity and common sense. The failure to clear Dr. Oppenheimer, he noted, will be a 'black mark on the escutcheon of the country.' Conservative in his politics and personal views, Dr. Evans had a refreshing tolerance for disagreement and idiosyncrasy once basic loyalty was established. He knew that a narrow conformity in thought and action produces stereotyped minds. He followed his own philosophy of tolerance, and those who were exposed to it will not soon forget him."

"Doc" (he was so universally known as "Doc" that, even here, it seems inappropriate to refer to him in any other way) entered his chosen profession somewhat late. He received his bachelor's degree from Franklin and Marshall in 1907 (and an honorary D.Sc. in 1932). Following graduation he taught high school for 6 years in Pennsylvania and New York before commencing graduate work at Columbia University. He was 36 when he was awarded the Ph.D., in 1916. He remained at Columbia for a year as Harriman fellow and then joined the faculty of the department of chemistry at Northwestern University, where

he remained until he became professor emeritus in 1945. During his last 3 years at Northwestern he was chairman of the department.

Doc was not one who retires easily. The following year he was with the U.S. Army University in France and England. He then became professor of chemistry at Loyola University in Chicago, from which institution he acquired his second title of professor emeritus, in 1956.

Between 1920 and 1942, Doc published about 20 scientific papers. The most important of these dealt with electrochemical studies of the structure of Grignard reagents. These papers are basic to the subject and are frequently referred to. A subject which occupied him in less formal ways was explosions. He became interested in these during a period with the Army during World War I. He was concerned with explosions, either as a member of committees or as a legal expert, until his death.

He was active in the affairs of the American Chemical Society. He was chairman of the Chicago Section for a year and a director and councilor of the section for many years. He also served a term as chairman of the Division of Physical and Inorganic Chemistry.

Small, wiry, and hardy, Doc was of the type who looks older than his age when young and younger when old. He was extremely shrewd in his judgment of facts, of men, and of fish. Shrewdness in the first two items stood him in good stead in the classroom and on the witness stand. His disarming manner and casual appearance (his hats were a Northwestern tradition, and one former student swears that he wore the same necktie every day for an entire year) led a number of opposing lawyers seriously to underestimate him, to their mortification when Doc finally sprang his bear trap. Shrewdness with regard to fish was developed in over 70 years' practice of his favorite sport on the lower stretches of the Susquehanna, where he fished as a boy and later had a summer home.

He was an unusually effective teacher and one whom students never forgot. If he took a particular interest in the brilliant students, he also took an almost desperate interest in the academic salvation of the backward. In teaching freshman chemistry, he held that one must first get the student's interest. To this end, he was a master of the functional use of the anecdote, of the vivid expression, and of the demonstration. He also held that a lecturer should be heard in the back row. In fact, his lectures could be heard in the next building. In teaching physical chemistry he aimed at the inculcation of exact thinking in that subject. He believed in assigning large numbers of difficult problems. With these rather different approaches, he was unusually successful in both courses.

Doc was active and prominent in university councils. He particularly enjoyed, and was very effective in, his dealing with students. For many years he was on the Northwestern University athletic committee and chairman of the committee dealing with the undergraduate publications.

ROBERT L. BURWELL, JR.
Northwestern University

News of Science

Nobel Prizes

The Karolinska Institutet, Stockholm, Sweden, has announced that Daniel Bovet, 50, head of the department of pharmacology at the Istituto Superiore di Sanità in Rome, has been awarded the 1957 Nobel Prize in physiology and medicine for work that has led to the development of sulfa drugs, antihistamines, and muscle relaxants. Bovet was born in Switzerland but became a naturalized Italian citizen in 1947. He is the first Italian to win the Nobel Prize in medicine and physiology since 1906. (Enrico Fermi won the physics prize in 1938).

While Bovet was working at the Pasteur Institute in Paris in 1932, Germany's Gerhard Domagk reported that prontosil, a dye product, could be used to kill bacteria that cause common infections. Bovet and his colleagues immediately set about breaking down prontosil, a complex chemical, and eventually isolated sulfanilamide, first of the modern antibiotic drugs. In the next few years Bovet synthesized many related compounds.

Then in 1937, with a Swiss colleague, Bovet produced the first antihistamine. In the next 4 years he conducted some 3000 experiments to work out the chemical formulas that are the basis for most of the antihistamines now widely prescribed for hay fever, eczema, asthma, and other allergies.

Next he turned his attention to a study of curare and the mechanism by which it paralyzes the muscles. It took him 8 years to isolate the essential ingredients from the impure mixtures used by South American Indians to poison darts. He developed a series of synthetic curare drugs that are now considered landmarks in the history of anesthetics—for example, succinylcholine, which is now in general use as a muscle relaxant during surgery on the chest and abdomen. Bovet, who is not listed in either the international or the Italian *Who's Who*, has never taken out a patent in his own name and has never benefited financially from the commercial exploitation of his findings.

This year's Nobel Prize in physics has been awarded by the Swedish Royal Academy of Sciences to two Chinese-born investigators, Tsung Dao Lee, 31, the youngest full professor at Columbia University, and Chen Ning Yang, 27, of the Institute for Advanced Study at Princeton, N.J. Neither is a United States citizen, but both are permanent residents. The two men were cited "for their penetrating investigation of the so-called parity laws which has led to important discoveries regarding elementary particles" [*Science* **123**, 185 (1 February 1957)]. Lee and Yang destroyed experimentally the long accepted "Principle of the Conservation of Parity."

The 1957 Nobel Prize in chemistry, also awarded by the Swedish Academy, will go to Sir Alexander Todd, 50, professor of organic chemistry at Cambridge University since 1944, and chairman of the British Advisory Council on Scientific Policy. He is being honored for his work on nucleotide coenzymes, which has been in progress for nearly 15 years. In an interview with the press, Sir Alexander explained that the contribution by him and his research team was the determination of the fundamental chemical structure of nucleic acids. He described the acids as the genic material that passes on genetic characteristics from the

mother cell to the offspring, and commented "When you know the structure of these things (the genes contained in the chromosomes in cell nuclei) you can begin to find out how they pass on characteristics. If you do that, you've gone a long way toward finding out what life is."

All the Nobel laureates are to receive their awards—a recognition certificate, a gold medal, and $40,000—in a ceremony that will take place in Stockholm on 10 December. The King of Sweden, Gustaf VI Adolf, will make the presentation.

NAS Congratulates Soviet Academy

Detlev W. Bronk, president of the U.S. National Academy of Sciences, sent the following congratulatory letter to A. N. Nesmeyanov, president of the U.S.S.R. Academy of Sciences, on 6 October, two days after the launching of Sputnik I.

"On behalf of the National Academy of Sciences of the USA, I wish to congratulate you and your Academy of Science of the USSR for the great achievement of placing an earth satellite in orbit. This is a brilliant contribution to the furtherance of science for which scientists everywhere will be grateful. I had the privilege of conveying in person these congratulations to Academician Blagonravov in Washington on Saturday morning, and will do so again tomorrow to Academician Bardin."

Physicist Denied Passport

The U.S. Court of Appeals for the District of Columbia has ruled in the case of Weldon B. Dayton, physicist of Corning, N.Y., that the Secretary of State may use confidential information in denying passports to people believed to be going abroad to advance the Communist movement. Dayton was accused of being active in Communist-front activities, associating with Communists, and wanting to go abroad "to engage in activities which will advance the Communist movement." It is reported that Dayton wanted to go to India to conduct research with Bernard Peters, a physicist who renounced his American citizenship and left the country to work at the Tata Institute for Fundamental Research in Bombay.

Dayton held that he had the right to confront witnesses who gave information against him. The State Department eventually told him the substance of the charges but would not reveal the identity of the informants, saying that this would compromise investigative sources and endanger national security.

In a 2-to-1 decision, this view was approved by Judge E. Barrett Prettyman and Judge Wilbur K. Miller. Prettyman wrote in his majority opinion that "the community interest makes [the decision] necessary." In a dissent, Judge Charles Fahy stated: "A finding that the denial is in the 'national interest' is too broad when the particular national interest is not broken down to come within the governing criteria." Dayton's attorney, Harry I. Rand, intends to appeal to the Supreme Court.

The appellate court's ruling was just the opposite of that taken in another passport case in November 1955 by District Court Judge Luther Youngdahl. In the case of Leonard Boudin, Youngdahl ruled out the use of secret evidence by the State Department in acting on passport applications. The Government appealed Youngdahl's ruling, but later avoided the issue and granted Boudin a passport when the case was rejected by the Court of Appeals because of a legal technicality.

Kabul Archeology Exhibit

The Museum of Kabul in Afghanistan is to be reorganized with the aid of a mission established by the United Nations Educational, Scientific and Cultural Organization. The museum contains archeological collections considered of first importance in the study of the art and civilizations of Asia.

The UNESCO mission will consist of a specialist from Switzerland, a specialist from France, and a specialist from Syria. It will be headed by M. Jean Gabus of Neuchatel, Switzerland, who is director of the Institute of Ethnology at the University of Neuchatel.

The President Names Killian

James R. Killian, president of Massachusetts Institute of Technology, has been named by President Eisenhower to the newly created post of special assistant to the President for science and technology. He is to take office immediately. The President said:

"This man, who will be aided by a staff of scientists and a strong advisory group of outstanding experts reporting to him and to me, will have the active responsibility of helping me follow through on the program that I am . . . outlining. . . . Through him, I intend to be assured that the entire program is carried forward in closely integrated fashion, and that such things as alleged interservice competition or insufficient use of overtime shall not be allowed to create . . . harm to our scientific and development program.

"Moreover, Dr. Killian will see to it that those projects which experts judge have the highest potential shall advance with the utmost possible speed. He will make sure that our best talent and the full necessary resources are applied on certain high-priority top-secret items. . . ."

In the television address on 7 November in which he announced Killian's appointment, the President discussed the U.S. missiles program and reported that this country had solved the problem of bringing a missile back from outer space. He also announced changes in the Defense Department to give missile development priority and to assure that "any new missile program . . . will, whenever practicable, be put under a single manager and administered without regard to the separate services." In conclusion, the President said:

"Although for tonight's purpose I stress the influence of science on defense, I am not forgetting that there is much more to science than its function in strengthening our defense, and much more to our defense than the part played by science. The peaceful contributions of science . . . are the most important products of the conquest of nature's secrets." . . .

U.S.–U.K. Conference on Controlled Thermonuclear Research

Major phases of research in the field of controlled thermonuclear reactions in the United Kingdom and the United States were reported upon and discussed recently in a joint conference of representatives of the two nations at Princeton University. The conference was arranged by the U.S. Atomic Energy Commission and the U.K. Atomic Energy Authority.

Several essentially distinct approaches to solving the problems of controlled thermonuclear reactions are being pursued in each of the two countries. Some of the experimental devices utilized have, for some months, been yielding substantial numbers of neutrons from the interior gas; in other machines there has been confinement of very hot gases for a small fraction of a second.

There are two main conditions necessary for the attainment of power-producing thermonuclear reactions. First, heavy hydrogen must be heated to a temperature of at least 100 million degrees centigrade. Second, this hot gas must be confined within a container for an appreciable fraction of a second. When the temperature reaches several million degrees centigrade, neutrons will be emitted in large numbers.

At this lower temperature, it is a delicate and difficult matter to distinguish

the neutrons produced by thermonuclear processes from those arising from other processes that are of no particular interest for controlled thermonuclear reactions. Since all neutrons are similar, their mode of origin has to be established by elaborate experiments. Such experiments are in progress in both countries.

Reports at the meeting in Princeton on the temperatures reached in the controlled thermonuclear experiments suggest that neutrons from thermonuclear reactions have been achieved, but more experimental work will be necessary to establish this as a fact. Realization of the objective of producing thermonuclear neutrons, if definitely established, would be an important step in the long-range effort to develop thermonuclear reactors for the production of economic power.

Development of Food Irradiation Reactor Suspended

The Atomic Energy Commission has suspended activities directed toward the design and construction of the Food Irradiation Reactor (FIR) and will terminate its contract with Kaiser Engineers, Oakland, Calif., for development work on this project. The reactor was being developed for use by the Army Quartermaster Corps in food irradiation experiments and other projects at the U.S. Army Ionizing Radiation Center, to be built at Stockton, Calif.

The Department of Defense has recently indicated an interest in the investigation of alternative sources of gamma irradiation, such as long-lived radioisotopes or spent reactor fuel elements. Pending the results of this investigation, the commission has suspended development work on the FIR.

Scripps Institution's Downwind Expedition

Two ships from the University of California's Scripps Institution of Oceanography have sailed on a 4½-month voyage to conduct studies in connection with the International Geophysical Year. The trip, called the Downwind Expedition, will take the research vessels *Horizon* and *Spencer F. Baird* to the southeast Pacific Ocean, scientifically one of the least known areas in the world. Henry W. Menard, Jr., associate professor of geology at the Scripps Institution, is scientific leader of the expedition, whose ports of call will include Tahiti; Pitcairn Island, settled by the *Bounty* mutineers; Robinson Crusoe's island, Juan Fernandez, off the coast of Chili; the South American ports of Valparaiso, Chile, and Callao, Peru; and Easter Island, noted for its mysterious stone statues.

However, only a few days will be spent in port, for the primary purpose of the expedition is to study how the deep waters of the ocean move. Practically nothing is known about deep currents because it is difficult and expensive to make measurements below the sea's surface, and effective methods have only recently been developed. In fact, so little is known about the circulation of the deep ocean water that nobody knows whether it takes 100 years or 10,000 for this water to travel from the Antarctic to the Equator and back again.

The expedition will also provide data for other IGY studies in the course of the more than 38,000-mile voyage. Twenty-five seismic stations will be occupied as part of the IGY seismological program. Samples for radiocarbon analysis of ocean waters will be taken from five locations. Such samples "date" ocean water. Air and water samples will be collected for analysis of carbon dioxide content.

In addition, the expedition's scientists will make a profile of the ocean floor along the line of 130° west longitude from the latitude of San Diego, Calif., to approximately 50° south. Several dredge hauls will be made to collect samples that will help determine the mineral resources of the sea floor. The atolls of the Tuamotu Archipelago will be studied.

One of the primary projects of the voyage will be investigation of the broad rises in the southeastern Pacific. Such rises are characteristic of all the oceans except the North Pacific, where most of the Scripps expeditions have been conducted. Surveys will also be made of the narrow, deep South American Trench just off the coast of Chile and Peru. The slope from the bottom of this trench to the crests of the adjacent Andes is the steepest in the world.

Scientists interested in joining the expedition at Valparaiso or Callao, or in having special observations or collections made, should communicate with Dr. Roger Revelle, University of California, Scripps Institution of Oceanography, La Jolla, Calif.

Golden Anniversary of the Pasteur Institute in India

This year marks the 50th anniversary of the Pasteur Institute in Kasauli, India. A souvenir volume published to celebrate the golden jubilee contains a tribute by its present director, N. Veeraraghaven, to the men who have guided the organization's development over the past half-century. Another section of the commemorative volume is devoted to a description of the institute's research activities, which have included significant work in the following areas: rabies, influenza, *Q*-fever, cholera, typhoid fever, diphtheria, fusospirochaetosis, serology of syphilis, tropical eosinophilia, malaria, leishmaniasis, venoms, and entomology.

Changes in vaccine for rabies and methods of production over the years are briefly described, and especial reference is made to the painstaking record-keeping, instituted by the first director and still maintained, of the history of hundreds of patients bitten by rabid animals, but untreated, considered in parallel with the results of treatment of persons bitten by the same animals. This continuing investigation is considered to be a unique record.

The last section is the scientific report of the institute for the year 1956. It describes an experimental evaluation of recent advances in antirabies treatment, an assessment of the value of 5 percent simple vaccine in human treatment, and studies on the cultivation of the rabies virus *in vitro*.

Postdoctoral Research Associateships

The National Academy of Sciences–National Research Council has announced that Postdoctoral Resident Research Associateships again will be offered for 1958–59 by the Argonne National Laboratory, the National Bureau of Standards, the Naval Research Laboratory, and the Oak Ridge National Laboratory. The associateships are tenable at the Argonne National Laboratory in Lemont, Ill.; at the Washington, D.C., and Denver, Colo., laboratories of the National Bureau of Standards; at the Naval Research Laboratory in Washington, D.C.; and at the Oak Ridge National Laboratory in Oak Ridge, Tenn.

These associateships have been established to provide young scientists of unusual ability with an opportunity for advanced training in basic research in the general areas of the biological, physical, and mathematical sciences. In addition, research associateships in visual psychophysics and engineering psychology are also available.

Applicants must be citizens of the United States. They also must produce evidence of training, in one of the listed fields, equivalent to that represented by the Ph.D. or Sc.D. degree and must have demonstrated superior ability for creative research. The stipend for these associateships is $7035 a year.

Application materials may be secured by writing to Fellowship Office, National Academy of Sciences–National Research

Council, 2101 Constitution Ave., Washington 25, D.C. In order to be considered for awards for 1958–59, applications must be filed at the Fellowship Office on or before *13 January 1958.*

News Briefs

The International Academy of Proctology has announced its annual cash prize and merit award for the best unpublished contribution on proctology or applied subjects. Contest entries must be received *before 1 February 1958,* by Alfred J. Cantor, International Secretary, International Academy of Proctology, 147–41 Sanford Ave., Flushing, N.Y.

* * *

The University of Wisconsin's botany and zoology departments are expanding their physical facilities for the first time in 45 years. They have begun to use the new $1,850,000 addition to Birge Hall, which was built in 1912. The new wing doubles the physical facilities of the two departments.

* * *

A $1-million science building was recently dedicated at Wilkes College. The building was named in honor of Admiral Harold R. Stark, who is a member of the board of trustees of the college. William L. Laurence, science editor of the *New York Times,* was principal speaker at the dedication dinner.

Scientists in the News

ERNEST O. LAWRENCE, Nobel laureate and director of the University of California Radiation Laboratory at Berkeley, will receive the Atomic Energy Commission's $50,000 Enrico Fermi Award on 2 December, the anniversary of the day when the late Dr. Fermi and his associates proved that nuclear fission could be self-sustained and controlled. Lawrence is being honored for his invention and development of the cyclotron and for his many other contributions to atomic energy and nuclear physics.

JAMES M. PRICE of the University of Wisconsin Medical School and SEYMOUR COHEN of the University of Pennsylvania are the first recipients of the American Cancer Society's new lifetime salary grants. These awards for two permanent faculty level positions in cancer research amount to $224,000 for the University of Pennsylvania and $392,296 for the University of Wisconsin.

TIEN-CHUAN WANG has recently joined Arthur D. Little, Inc., Cambridge, Mass., and is working in its Advanced Research Division in the field of microwave physics. He was formerly a member of the group at Columbia University which conducted research that led to the successful development of the ammonia maser. Before coming to the United States Wang taught and did research in electronic physics at several universities and institutes on the Chinese mainland. He has specialized in nuclear resonance and microwave spectroscopy.

VIRGIL P. SYDENSTRIKER has been named emeritus professor and emeritus chairman of the department of medicine of the Medical College of Georgia. He had served as professor of medicine for 35 years. Since his retirement last summer, he has been appointed to the staff of the Veterans Administration Hospital in Augusta, Ga.

GIAMPIETRO PUPPI, director of the Institute for Physics at the University of Bologna, is a visiting professor in the physics department of the University of Maryland for the fall semester, 1957–58. In the spring and summer semesters, Cyril Domb, professor of theoretical physics at the University of London, will be a visiting professor.

DONALD E. THOMAS and KENNETH M. GOLDMAN, metallurgists at the Bettis atomic power division of the Westinghouse Electric Corporation, have received special company awards of $2000 each for the discovery in 1952 of a broad range of zirconium alloys that have a high corrosion resistance and are therefore especially capable of withstanding the high temperature and pressure generated in atomic power plants. The discovery helped solve one of the major problems in the design and development of the reactor for the *U.S.S. Nautilus.*

ARTHUR C. ALLEN, formerly associate pathologist at the Memorial Center for Cancer and Allied Diseases and associate professor of pathology at Cornell University Medical School, Sloan-Kettering Division, has accepted appointment as professor of pathology at the University of Miami Medical School and attending pathologist at the Jackson Memorial Hospital.

WILLIAM H. FORSTER, associate director of research in charge of semiconductor research and development at the Philco Corporation, Philadelphia, has been named director of research in charge of the newly formed solid state electronics department of the company's Research Division. CARLO V. BOCCIARELLI is assistant director of research for the new department.

GIUSEPPE BERTANI, geneticist and for the past 3 years a senior research fellow in biology at California Institute of Technology, has been appointed associate professor of medical microbiology at the University of Southern California.

The following staff changes have taken place in the department of geology and geophysics at Massachusetts Institute of Technology.

WALTER L. WHITEHEAD retired last June, but continued as director of the 1957 M.I.T. Summer School of Geology at Crystal Cliffs, Nova Scotia, and has been appointed lecturer in geology at M.I.T. and visiting professor at St. Francis Xavier University, Antigonish, Nova Scotia.

HERBERT E. HAWKES resigned to accept a professorship in the Division of Mineral Exploration, University of California (Berkeley).

WILLIAM S. VON ARX and J. BRACKETT HERSEY, physical oceanographers at Woods Hole Oceanographic Institution, have been appointed associate professors.

HARRY HUGHES, scientific officer, United Kingdom Atomic Energy Authority, is visiting lecturer in geophysics during the present school year.

In the department of meteorology, NORMAN A. PHILLIPS has been appointed associate professor.

PHILIP S. HOPKINS, professor of aviation and head of the department of aviation at Norwich University, Northfield, Vt., has been appointed director of the Smithsonian Institution's National Air Museum.

WILLIAM H. FELDMAN, a member of the staff of the Mayo Foundation and Mayo Clinic since 1927, has accepted a post as chief of laboratory research in pulmonary diseases in the department of medicine and surgery of the Central Office Staff, Veterans Administration, Washington, D.C.

C. D. W. THORNTON has been named director of research and development at Farnsworth Electronics Company, Fort Wayne, Ind. Before he joined the company as assistant to the president for atomic energy in 1956, Thornton had been chief of the Office of Operations Analysis and Planning for the U.S. Atomic Energy Commission in Washington, D.C.

The following awards will be presented in New York next March during the annual meeting of the Institute of Radio Engineers.

ALBERT W. HULL, a consultant to the General Electric Research Labora-

tory in Schenectady, N.Y., will receive the Medal of Honor, highest technical award in the radio-electronics field "for outstanding scientific achievement and pioneering inventions and development in the field of electron tubes."

W. R. G. BAKER, vice president of General Electric Company, will receive the Founders Award, which is bestowed "for outstanding contributions to the radio engineering profession."

EDWARD L. GINZTON, professor of applied physics and electrical engineering at Stanford University, will receive the Morris Liebman Memorial Prize "for his creative contribution to the generation and useful application of high energy at microwave frequencies."

EDWARD W. ALLEN, JR., chief engineer of the Federal Communications Commission, will receive the Harry Diamond Memorial Award "for his technical and administrative contributions in the field of radio spectrum utilization."

CHARLES P. GINSBURG, of the Ampex Corporation, Redwood City, Calif., will receive the Vladimir K. Zworykin Television Prize "for pioneering contributions to the development of video magnetic recording."

GEORGE SACHS, professor of metallurgical engineering and associate director of Syracuse University's Research Institute, will receive an honorary doctor of engineering degree at the commencement of the Bargakademie (school of mines) at Clausthal, West Germany, on 5 May 1958. Sachs graduated from the Berlin Engineering School and was a director of metals research for Metallgesellschaft, in Frankfurt, Germany, before he came to this country in 1936.

ALLEN C. MUNSTER, mathematician who joined the Philco Corporation, Philadelphia, in 1944, has been named associate director of research at Philco. His responsibilities will center on the technical direction and administration of Government and industrial research programs.

KENNETH A. DUNBAR, manager of the Atomic Energy Commission's area office in Portsmouth, Ohio, has been named manager of the Chicago Operations Office of the AEC at Lemont, Ill., effective 1 December. He succeeds JOHN J. FLAHERTY, who resigned on 1 October to return to private industry.

CARL LAMANNA, formerly of the School of Hygiene and Public Health at Johns Hopkins University, has been appointed scientific director of the Naval Biological Laboratory and the affiliated Naval Medical Research Unit No. 1 at the University of California in Berkeley.

JAMES W. CULBERTSON, professor of medicine and director of the Cardiovascular Research Laboratories at the State University of Iowa College of Medicine since 1949, will join the staff of the University of Tennessee as professor of medicine, effective next spring.

Also at Tennessee, WILLIAM H. L. DORNETTE, assistant professor of anesthesiology at the University of California Medical Center, Los Angeles, will become professor and head of the department of anesthesiology on 1 January 1958.

H. F. ROBERTSON, who has been associated with the Union Carbide Corporation since 1926, has been appointed technical director of the Union Carbide Development Company, a division of the corporation. For the past 13 years he has served in various capacities at the Bakelite Company, another Union Carbide division, where he became manager of technical planning in 1956.

GEORGE A. THIEL, chairman of the geology and mineralogy department at the Univeristy of Minnesota, has been selected as outstanding geology teacher of the year by the Association of Geology Teachers. He received the 1957 Neil Miner Teaching Award at the association's fall meeting, which took place recently in Atlantic City in conjunction with the Geological Society of America's annual meeting.

ABSOLOM VILAKAZI, Zulu anthropologist and educator from Johannesburg, South Africa, has been appointed professor of African studies at the Kennedy School of Missions of the Hartford (Conn.) Seminary Foundation. Vilakazi and his family arrived in this country on 12 November.

CLARENCE F. WINCHESTER, animal physiologist at the U.S. Department of Agriculture's Agricultural Research Center, Beltsville, Md., has accepted a 2-year appointment by the International Cooperation Administration as livestock adviser to the Government of Ceylon. He will be stationed at Ceylon University, in Peradeniya.

GEORGE R. JOHNSON, associate professor of animal science at Ohio State University's College of Agriculture, has been promoted to professor and chairman of the department, effective 1 January 1958. He will also serve as chairman of animal science at the Agricultural Experiment Station. Johnson will succeed LAWRENCE A. KAUFFMAN, chairman since 1955, who has asked to be relieved of administrative duties but who will continue on the animal science faculty.

MANUEL R. MALINOW of the University of Buenos Aires, Argentina, has been appointed visiting professor in physiology at the State University of New York, Downstate Medical Center, from October 1957 through March 1958.

Recent Deaths

SOLOMON F. ACREE, Washington, D.C.; 81; organic research chemist; former chief of a section for acidity measurements at the National Bureau of Standards; 23 Oct.

ALBERTO ASCOLI, Milan, Italy; 80; professor emeritus of the University of Milan; pioneer in the use of B.C.G., founder of the Italian Institute for Anti-Tuberculosis Vaccination; 28 Sept.

ALPHEUS BLIZZARD, Hartsville, S.C.; biologist and retired member of the staff of the plant quarantine section of the U.S. Department of Agriculture; former chairman of the department of biology at Coker College; past president of the South Carolina Academy of Science; 19 Oct.

GERTY T. CORI, St. Louis, Mo.; 61; professor of biological chemistry at Washington University; shared the 1947 Nobel prize for studies on the body's use of starches and sugars (with her husband, Carl, and with B. A. Houssay of Argentina); internationally known for her work on enzymes and carbohydrate metabolism; 26 Oct.

FRANK G. DAVIS, Lewisburg, Pa.; professor emeritus of education at Bucknell University and the author of a number of books on counseling and guidance; 21 Oct.

JOSEPH FERGUSON, Philadelphia, Pa.; 50; electrical engineer who has been associated with the Nickel Processing Corporation of New York, supervising the company's construction in Cuba and Colombia; during World War II he coordinated the work of Pan American World Airways' engineers; 23 Oct.

WELLINGTON D. JONES, Chicago, Ill.; 71; professor emeritus of geography of the University of Chicago; specialist in soil geography, world classification of agricultural regions, and the geography of India and the Far East; first appointed to Chicago faculty in 1914; 24 July.

INA A. MARSH, Buffalo, N.Y.; 54; practicing psychiatrist and neurologist; assistant professor of neurology at the University of Buffalo Medical School; 21 Oct.

HENRY A. PILSBRY, Philadelphia, Pa.; 94; curator of mollusks at the Philadelphia Academy of Natural Sciences, with which he had been associated since 1887; author of many papers and of a two-volume work on *Land Mollusca of North America*; 26 Oct.

Reports

Oxygenated Ferroheme Proteins from Soybean Nodules

Twenty years ago, the discovery of a red pigment in legume nodules actively fixing atmospheric nitrogen provided a fresh approach to a problem of biology which merits far more than academic interest. Nodules, developing from roots underground in response to specific bacterial infection, to which bacteria they remain host, collectively constitute a plant organ responsible for all molecular nitrogen fixation by legume crops. Studies soon revealed that the nodule pigment is somehow associated with nitrogen fixation and, moreover, that it is an iron porphyrin protein remarkably like the vertebrate hemoglobins. But whereas in crude preparations the pigment could be reversibly deoxygenated, always during purification it became oxidized to the ferric state; thus upon purification it lost the ability to function as a stable oxygen carrier and lost, thereby, its qualification for classification as a hemoglobin. The instability thus evidenced in the presence of molecular oxygen, albeit during processing, cautions against prematurely categorizing the new pigment with the hemoglobins and so attributing to it a function, insufficiently demonstrated, which could be nonphysiological.

While most of these early studies were made on preparations of unresolved pigment, two components were ultimately fractionated by electrophoresis and analyzed (*1*). It was concluded that one native protoporphyrin protein of molecular weight approximately 20,000 and having approximately 0.3 percent iron had been isolated in its ferric state along with an artifact of twice this size.

The following account of the nodule pigment summarizes additional information from new studies, carried out over the past few years, culminating in the isolation of several oxygenated heme proteins from the soybean nodule and suggesting extensive research not only into nodule physiology but also into porphyrin-protein chemistry and physiology (*2*).

Three, and possibly four, ferro-protoporphyrin proteins can be isolated from fresh or frozen nodules of the soybean, *Glycine max*, two of these in abundance (*3*). An essential feature of isolation is rapid processing with controlled temperature and *p*H. Extraction is made by alkaline buffer in a blender, preferably under a stream of hydrogen or nitrogen; fractionation, by ammonium sulfate precipitation, preferably under H_2 or N_2, dialysis, and paper electrophoresis. The two major pigments, designated the *fast* and the *slow* from their respective rates of migration during electrophoresis, have been studied rather extensively.

Even 1-year-old frozen nodules and 1-year-old frozen ammonium sulfate pastes of crude pigment will yield ferro-pigments, but the dialyzed pigment mixture prepared for electrophoresis deteriorates rapidly. The isolated components disintegrate more slowly.

The first step recognized in pigment breakdown is the oxidation of the iron to its ferric state. Since the red, oxygenated pigments separate from their respective brown, oxidized, phases during electrophoresis, progress in oxidation is easily ascertained. In a fresh preparation, little (and, ideally, no) oxidized pigment is present; ultimately, no oxygenated pigment remains. Upon standing, the ferric-components progressively disintegrate to electrophoretically mobile, greenish fragments. Concurrently, denaturation and sedimentation of heme protein occurs.

Satisfactory methods of preservation have not been developed. Deterioration is retarded at low temperatures and in concentrated solutions, especially those containing ammonium sulfate. The use of reductants and antioxidants has not been favored because of the undesirability of complicating an already complex mixture.

The absorption spectra of the oxygenated ferro-pigments are similar, and are typical of oxygenated hemoglobins, with maxima at about 575, 540, and 412 mμ. However, whereas crystalline human oxyhemoglobin, as a reference standard, has an α/β (peak) ratio of 1.05 and an α (peak)/560 (minimum) ratio of 1.70, the freshly separated, oxygenated nodule pigments display diminished ratios of 0.99 and 1.35, respectively. Thus their spectra suggest, by analogy, the possibility of contamination with deoxygenated or, more likely, ferri-pigment; the ratios decrease daily and the spectra reveal a slow transition to the ferric state, with its weaker absorption, which is *p*H dependent, at about 570, 540, and 410 mμ. The maxima of the deoxygenated ferro-spectra lie at about 557 and 424 mμ.

The oxygenated ferro-pigments can be reversibly deoxygenated by chemical means or, similarly, the ferri-pigments can be reduced and oxygenated, but under restricted conditions—for example, when the reductant is promptly removed by electrophoresis. The easily reversible oxygenation of vertebrate hemoglobins has not been observed; instead, oxidation to the ferric state ensues. In alkaline media this oxidation could be mistaken for oxygenation simply because the ferri-pigment in its alkaline form absorbs light of almost the same wavelength as does the oxygenated pigment, though more weakly. Ease of oxidation appears in part to be due to the narrower range of *p*H stability clearly demonstrated by the nodule pigments.

As with ferri-hemoglobin, cytochrome *c*, or acid-base indicators in general, acid-base titration of the ferri-pigments can be followed spectrophotometrically (*4*); like cytochrome *c*, each pigment reveals several heme-linked acids: one of these dissociates reversibly with a *pK* of approximately 8.2, and four dissociate reversibly between *p*H 7 and *p*H 4 with more overlap than permits accurate *pK* analysis. Below *p*H 4, extensive molecular changes occur. Upon aging, the pigments are not titratable below *p*H 7, suggesting an impedance to electron-pair orientation about the porphyrin nucleus. Spectrophotometric titration also suggests a mesomerism which is seen to a lesser extent in the titration spectra of vertebrate hemoglobins.

The alkaline ferro-hemochromogen, the cyan-met, and the porphyrin dimethyl ester derivatives of the unresolved nodule pigment present typical protoporphyrin spectra. The protein moiety split from the hemin of the crude pigment recombines with vertebrate hemin and yields the composite electrophoretic pattern typical of the nodule pigment.

The molecular weights of the two major components are estimated, by dry-weight and heme-iron analysis, to be between 14,000 and 23,000 per heme unit.

All technical papers and comments on them are published in this section. Manuscripts should be typed double-spaced and be submitted in duplicate. In length, they should be limited to the equivalent of 1200 words; this includes the space occupied by illustrative or tabular material, references and notes, and the author(s)' name(s) and affiliation(s). Illustrative material should be limited to one table *or* one figure. All explanatory notes, including acknowledgments and authorization for publication, and literature references are to be numbered consecutively, keyed into the text proper, and placed at the end of the article under the heading "References and Notes." For fuller details see "Suggestions to Contributors" in *Science* 125, 16 (4 Jan. 1957).

Iron concentrations approximate 0.3 percent. Electrophoretic mobilities of the *fast* and the *slow* components were measured in the Tiselius apparatus as -0.43 and -0.30 μ cm^{-1}/v cm^{-1}, respectively, at *p*H 8.5 (Veronal, 0.1 μ) and as -0.32 and -0.20 μ cm^{-1}/v cm^{-1}, respectively, at *p*H 6.0 (phosphate, 0.1 μ) (*5*).

The role of the heme proteins in the legume nodule has not been elucidated; it must be remembered that oxygenation may be fortuitous, and that the several components need not be physiologically unique.

E. Thorogood*

Department of Bacteriology, University of Illinois, Urbana

References and Notes

1. N. Ellfolk and A. I. Virtanen, *Acta Chem. Scand.* **4**, 1014 (1950); **6**, 411 (1952).
2. This investigation was suggested and supported by D. L. Drabkin of the biochemistry department of the Graduate School of Medicine, University of Pennsylvania. The cooperation of the botany department of the University of Pennsylvania, and of the bacteriology department and the biochemistry division of the chemistry department of the University of Illinois, where parts of the research were conducted, is also gratefully acknowledged. The research has been supported, in part, by contracts between the Office of Naval Research and the University of Pennsylvania, between the National Science Foundation and the University of Illinois, and between the National Institute of Allergy and Infectious Diseases of the U.S. Department of Health, Education, and Welfare and the University of Illinois. More detailed descriptions of these studies are in preparation.
3. Paul Feltman, formerly of the University of Illinois, assisted in developing these oxygenated preparations.
4. E. Thorogood, *Chromoproteins from Soybean Nodules* (University of Pennsylvania, Philadelphia, 1955).
5. These analyses were performed by J. H. Custer, USDA Agricultural Research Station, Eastern Utilization Research Branch, Philadelphia, Pa., through the courtesy of T. L. McMeekin and C. A. Zittle.
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20 June 1957

Role of Glycolysis in Fatty Acid and Cholesterol Synthesis in Normal and Diabetic Rats

It has been repeatedly demonstrated that depressed glucose oxidation, as seen in such conditions as fasting or diabetes, results in marked derangements of fatty acid and cholesterol synthesis (*1*). That such disturbances in the synthesis of lipids are clearly secondary to the lack of glycolysis is shown by the fact that reinstitution of carbohydrate breakdown, by whatever means, results in prompt return of lipid synthesis to normal (*1*). Despite these well-demonstrated relationships, neither the sites of such metabolic lesions in fatty acid and cholesterol synthesis nor the mechanism by which glycolysis repairs them is known.

It is now well established that glucose oxidation can take place by either of two routes, the classical Embden-Meyerhof (EM) pathway or the more recently described hexosemonophosphate (HMP) shunt (*2*). While most glucose molecules are oxidized via the Embden-Meyerhof route (*2*), it seems possible that the hexosemonophosphate pathway might play a role in the *control* of cholesterol and fatty acid synthesis out of proportion to its quantitative importance in glycolysis.

Similar views concerning the control of fatty acid synthesis in normal animals have been suggested by the work of Brady in pigeon liver (*3*) and by the studies of Langdon in rat liver (*4*). A role of the hexosemonophosphate shunt in the lipogenic defect of the diabetic has not been previously established.

The present studies (*5*) were designed, first, to determine which of the two pathways of glucose oxidation is primarily responsible for the influence of glycolysis upon lipid synthesis in normal and diabetic animals and, second, to elucidate the mechanism by which such effects might occur.

Use was made of the facts, originally demonstrated by Wenner *et al.* (*6*) and confirmed by us (*7*), that, in tissue homogenates, glucose oxidation via the Embden-Meyerhof pathway is enhanced by the addition of diphosphopyridine nucleotide (DPN), while oxidation via the hexosemonophosphate shunt is stimulated by triphosphopyridine nucleotide (TPN). By adding the appropriate cofactor and simultaneously measuring the rates of lipid synthesis by acetate-1-C^{14} incorporation, the influence of each of these pathways upon fatty acid and cholesterol synthesis can, therefore, be determined.

As prepared, homogenates from normal animals were found to synthesize fatty acids at significant rates even in the absence of added coenzymes (Table 1). Stimulation of Embden-Meyerhof glycolysis caused a moderate increase in fatty acid synthesis (two- to threefold); in contrast, however, stimulation of the hexosemonophosphate shunt consistently produced a striking acceleration of from 30- to 100-fold. Stimulation of both pathways usually increased still further the rate of fatty acid synthesis.

The production of cholesterol would also seem to be greatly dependent upon the route of glycolysis. Whereas stimulation of the Embden-Meyerhof pathway alone produced negligible changes in the rate of synthesis of this sterol, hexosemonophosphate oxidation caused a marked increase of at least 40- to over 100-fold. In contrast to the case of fatty acid synthesis, however, addition of Embden-Meyerhof glycolysis to hexosemonophosphate oxidation depressed cholesterol synthesis relative to that seen when the shunt alone was stimulated.

It appears, therefore, that in the system under study, it is the glucose that is oxidized via the hexosemonophosphate shunt that is primarily responsible for the effects of glycolysis in enhancing both fatty acid synthesis and cholesterol synthesis in normal liver. It would also follow that, when glucose is being oxidized at an adequate rate, cholesterol synthesis might be controlled by the relative amounts of glucose that traverse each of the glycolytic pathways—that going by the hexosemonophosphate shunt stimulating the process, and that using the Embden-Meyerhof pathway depressing it.

The explanation for these effects was suggested by Langdon's finding that reduced TPN (TPNH), which is known to be produced by the hexosemonophosphate shunt but not by the Embden-Meyerhof pathway, is required in the synthesis of fatty acids at the point of conversion of crotonyl-CoA to butyryl-CoA (*9*). We would suggest that TPNH is also required or is at least rate-limiting in cholesterol biogenesis. A requirement for TPNH in both of these syntheses, then, makes it likely that it is this cofactor, and not some other product of hexosemonophosphate stimulation, that mediates the effect of hexosemonophosphate oxidation on lipid synthesis. This is probably the

Table 1. Effect of glycolytic pathway upon cholesterol and fatty acid synthesis. Two milliliters of cell-free homogenates of normal or alloxan diabetic rat liver, prepared with an equal volume of 0.1*M* K_2HPO_4 buffer, was incubated under an atmosphere of 95 percent O_2 and 5 percent CO_2 for 1 hour at 37°C. Glucose-6-phosphate ($18 \times 10^{-3}M$) served as the intermediate common to both pathways of glucose oxidation. Other cofactor concentrations were as follows: DPN, $0.7 \times 10^{-3}M$; TPN, $0.7 \times 10^{-3}M$; isocitrate, $18 \times 10^{-3}M$; acetate, $1.9 \times 10^{-3}M$. Fatty acids and cholesterol were isolated as previously described (*8*) and were assayed by liquid scintillation counting. EM, Embden-Meyerhof pathway; HMP shunt, hexosemonophosphate shunt.

Glycolytic pathway stimulated	Normal		Diabetic	
	Acetate-C^{14} recovered in		Acetate-C^{14} recovered in	
	Fatty acids (mμ-mole)	Cholesterol (mμ-mole $\times 10^{-2}$)	Fatty acids (mμ-mole)	Cholesterol (mμ-mole $\times 10^{-2}$)
Neither	0.5	< 3	< 0.1	< 3
EM	1	< 3	< 0.1	< 3
HMP shunt	29	212	73	302
Both	53	98	302	309
Neither	1	< 3	< 0.3	< 6
EM	3	12	1.2	< 6
HMP shunt	120	123	28	62
Both	224	73	263	52
Neither	4	7	< 0.3	< 6
EM	4	10	0.6	< 6
HMP shunt	133	962	30	754
Both	224	385	88	1066
Isocitrate + TPN	314	505	166	400

case since another TPNH-generating system, D-isocitrate and TPN, is also capable of producing a marked stimulation of fatty acid and cholesterol synthesis (Table 1).

That the well-established defect in fatty acid synthesis seen in the diabetic state is likewise due to a lack of glucose oxidation via the hexosemonophosphate shunt is demonstrated in Table 1. The lesion observed in the intact animal and in the liver slice (*1*) is also demonstrable in liver homogenates (see also *10, 11*). By stimulation of the hexosemonophosphate shunt, however, fatty acid synthesis in the diabetic can be restored approximately to the same level as it is in many normal livers. This increase represents a stimulation of diabetic lipogenesis of at least 100- to 700-fold. As in the normal liver, further enhancement of fatty acid synthesis is seen when both pathways are stimulated. For reasons which are not yet clear, cholesterol synthesis in the diabetic, while stimulated by hexosemonophosphate oxidation, was not relatively depressed by the addition of Embden-Meyerhof glycolysis.

That the defect in lipogenesis found in the diabetic liver is likewise primarily due to a deficiency of TPNH is supported by the fact that the alternate TPNH-generating system, D-isocitrate and TPN, will largely correct this lesion (Table 1). It would follow, therefore, that the primary diabetic block in fatty acid synthesis is at the site of action of TPNH—namely, at the reduction of crotonyl-CoA to butyryl-CoA (*9*). The location of this diabetic block at some point prior to the involvement of butyryl-CoA was previously indicated by the finding of Shaw, Dituri, and Gurin that butyryl-CoA can stimulate fatty acid synthesis in diabetic liver (*11*).

Finally, evidence that the conclusions drawn from these *in vitro* studies are applicable to the intact animal is the observation that diabetic acidosis is characterized by an accumulation of the ketone bodies, beta-hydroxybutyric and acetoacetic acids, the CoA derivatives of which are two of the fatty acid precursors preceding the blocked TPNH-requiring step.

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2 August 1957

Significance of the Malate Synthetase Reaction in Bacteria

An alternate pathway of malic acid synthesis has been discovered in our laboratories. An enzyme, named "malate synthetase," has been obtained from *Escherichia coli*, strain E26, that is grown on acetate. This enzyme converts equimolar concentrations of acetate and glyoxylate to malic acid (*1*).

Purification of malate synthetase by several ammonium sulfate precipitations and treatment with calcium phosphate gel and protamine sulfate resulted in a 50-fold purification with an approximate 30 percent yield. The final product was free of fumarase, Ochoa's condensing enzyme, isocitritase, and glyoxylate reductase. Experiments conducted with such preparations revealed that for each mole of acetyl phosphate and glyoxylate that disappears, 1 mole of malate is formed. With acetyl phosphate as substrate, coenzyme A (CoA) (*2*) and phosphotransacetylase are required. These can be replaced with acetyl-CoA. The formation of malic acid can thus be formulated as follows:

$$\text{Acetate} + \text{ATP} \rightarrow \text{acetyl phosphate} + \text{ADP} \quad (1)$$

$$\text{Acetyl phosphate} + \text{CoA} \xrightarrow{\text{transacetylase}} \text{acetyl-CoA} + \text{PO}_4 \quad (2)$$

$$\text{Acetyl-CoA} + \text{glyoxylate} \xrightarrow[\text{synthetase}]{\text{malate}} \text{malic acid} + \text{CoA} \quad (3)$$

To demonstrate the initial reactants in reaction 3, acetyl-CoA was synthesized chemically from thiolacetate and CoA and was incubated in the presence of glyoxylate and malate synthetase. Analysis of the reaction mixture, after the incubation period, revealed that malate was quantitatively formed. Magnesium ions were routinely added, but it has not yet been definitely ascertained that they are required.

The equilibrium of the over-all reaction is overwhelmingly in favor of malate synthesis. Attempts to demonstrate the reversibility of this reaction have failed thus far.

Malate synthetase appears to be an adaptive enzyme, for it was found only in cells that have been grown on acetate as the major carbon source. It has thus far been found in acetate-grown *E. coli, Aerobacter aerogenes, Corynebacterium creatinovorans,* and *Pseudomonas fluorescens.* When any of these organisms were grown on substrates other than acetic acid, malate synthetase could not be detected.

The significance of the occurrence of malate synthetase in nature (*3*) stems from the fact that it fills in a significant gap in our knowledge of carbohydrate metabolism in that it explains the long baffling problem concerning the mechanism by which bacteria can grow on two-carbon compounds such as acetic acid. Assume that cells, when first exposed to acetate as the sole carbon source, contain, as they do, minimal catalytic amounts of oxalacetate. This being the case, the first event to occur would be a combination of acetate and oxalacetate to form citrate. The latter could then be cleaved by way of isocitrate to succinate and glyoxylate. The glyoxylate formed would in turn condense with another molecule of acetate via the malate synthesis reaction, forming a *new* C_4 unit. The net result during this process, assuming no drainage to supply carbon skeletons for amino acid synthesis, would be a gain of one C_4 unit, as is shown in Fig. 1. Thus, by assuming the presence of even *one* molecule of oxalacetate, all acetate carbon could be converted to C_4 units as follows:

$$\text{Isocitrate} + \text{acetyl-CoA} \rightarrow \text{malate} + \text{succinate}$$

Further, since growth occurs on acetate as the sole source of carbon, intermediates are constantly being drained from the tricarboxylic acid cycle and utilized for amino acid synthesis. Under these conditions, rapid net synthesis of C_4 dicarboxylic acids is therefore required to provide the acceptor for the C_2 units entering the cycle. The malate synthetase reaction meets that need completely. This reaction, *in vitro,* at least, is rapid and proceeds almost exclusively in the direction of malate formation. In addition, as was pointed out earlier, the system is adaptive—that is to say, malate synthetase forms only when cells are grown on acetate as the sole carbon source. This suggests the enzyme is important primarily when C_2 intermediates are involved. Energy for synthesis during growth is, as illustrated in Fig. 1, un-

doubtedly provided by the conventional oxidation of isocitrate via the tricarboxylic acid cycle reactions. The predominant flow of any one of these pathways would of course be determined by the total economy of the cell at any moment during growth.

Now, suppose that the hypothetical situation exists in which no endogenous oxalacetate is available to the cells. Under these conditions, growth on acetate could be explained if an enzyme were present in bacteria which would bring about the direct conversion of acetate to glyoxylate via glycolate, not involving a C_6 intermediate, such as isocitrate. If this were the case, cells exposed to acetate would initially convert enough of this C_2 unit to glyoxylate in order to provide the appropriate C_2 unit for the formation of malic acid via the malate synthetase reaction. Once this process has been initiated, it could continue until all the acetate is utilized for both synthesis and energy. However, here again, when bacteria are grown on acetate, intermediates are being drained from the tricarboxylic acid cycle for synthetic reactions. Rapid synthesis of C_4 acids is therefore again required to provide acceptors for the C_2 units entering the cycle.

It is known that the condensation of CO_2 with pyruvate is one of the intermediate reactions in the synthesis of C_4 compounds. However, the quantitative significance of this reaction during growth of bacteria on C_2 units is not altogether apparent. Neither is the formation of the C_3 unit via a two-carbon compound and CO_2 apparent. Therefore, the direct formation of glyoxylate from acetate and the subsequent condensation of the latter acid to malate would indeed provide a source of readily available C_4 units.

A portion of this problem, the formation of malic acid via malate synthetase, has been solved. However, the conversion of acetate to glyoxylate not involving a C_6 intermediate has not yet been adequately demonstrated. That this reaction occurs in bacteria and yeast has been claimed by Bolcato and coworkers (*4*). However, their data do not completely exclude the possibility that glyoxylate arises by presently known mechanisms involving C_6 intermediates. Thus, with resting cells, which these investigators have used, acetate could readily combine with endogenous oxalacetate to form citrate. The latter acid, via isocitrate, could be cleaved to glyoxylate and succinate. Thus, we have the formation of glyoxylate from acetate. The data of Bolcato do not exclude this possibility.

In conclusion, it can be said that the malate synthetase reaction provides a rational explanation for the mechanism by which bacteria such as *E. coli* grow on acetate as a sole source of carbon, provided that the assumption is made that the organisms have within them catalytic quantities of oxalacetate to initiate the following processes:

$$\text{Acetate} + \text{oxalacetate} \rightarrow \text{citrate} \rightarrow \text{isocitrate} \quad (4)$$

$$\text{Isocitrate} \rightarrow \text{succinate} + \text{glyoxylate} \quad (5)$$

$$\text{Glyoxylate} + \text{acetate} \rightarrow \text{malate} \quad (6)$$

Reactions 5 and 6 may be summarized as follows:

$$\text{Isocitrate} + \text{acetate} \rightarrow \text{succinate} + \text{malate}$$

On the other hand, assuming that catalytic amounts of oxalacetate are not available, a mechanism for C_4 acid-formation needs to be postulated. Known CO_2 fixation reactions alone do not explain the formation of a C_4 compound from a C_2 unit, although the participation of CO_2 in the formation of C_4 units from acetate has been recently suggested by the experiments of Kornberg (*5*).

The mechanism by which bacteria grow on C_2 carbon units other than acetate is now also being elucidated. Thus Krakow and Barkulis (*6*) discovered a reaction wherein two molecules of glyoxylate are involved in the formation of a C_3 unit, presumably hydroxypyruvate, and CO_2. Here the situation appears to be considerably less complex than in the case of acetate. Assuming that hydroxypyruvate can be readily converted to pyruvate via known CO_2 fixations, oxalacetate is formed, and a steady supply of C_4 acids is thus provided. Malate synthetase could play a role in the growth of bacteria on glyoxylate by providing an additional route of C_4 acid formation, but only after acetate has been produced from pyruvate.

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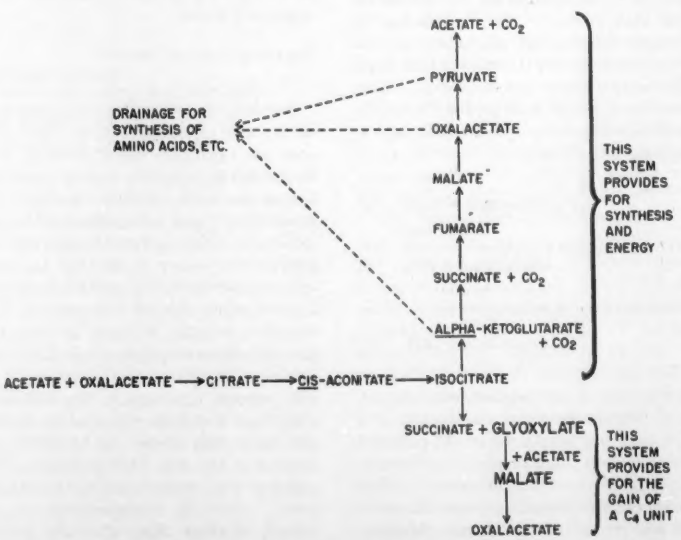

Fig. 1. Growth of bacteria on acetate.

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5 July 1957

Oxidation of Serotonin in the Presence of Ceruloplasmin

The metabolism of serotonin leads to the formation of 5-hydroxyindoleacetic acid (*1*). However, there are other possible metabolic pathways which might bear a relationship to the physiological activity of serotonin. One of these is oxidation of the molecule to yield a *p*-quinone imine derivative, a reaction which should be catalyzed by the copper-protein enzyme, ceruloplasmin (*2*). Further oxidation or hydroxylation, enzymatic or "nonspecific" (*3*), of the *p*-quinone imine could result in compounds structurally related to adrenochrome.

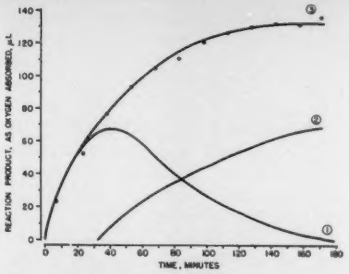

Fig. 1. Oxidation of serotonin in the presence of ceruloplasmin. Reaction rates were derived from spectrophotometric and oxygen-consumption data. Curve 1, product of the first oxidation (p_1); curve 2, product of the second oxidation (p_2); curve 3, total oxygen consumption ($p_1 + 2p_2$); the dots show observed oxygen consumption.

Ceruloplasmin concentrates were obtained by further alcohol and salt fractionation of Cohn's fraction IV-1, method 6 (*4*), from pooled human plasma. Preparation 49, which was used in the experiments described here, contained 0.23 g of copper and 1.23 g of protein per 100 ml. Thus, the enzyme had a purity above 50 percent (*2*). However, its catalytic properties were identical with those of more highly purified (90 percent) concentrates.

Three-tenths of a milliliter of enzyme solution and 2.2 ml of 0.1*M* acetate buffer, *p*H 6.00 ± 0.01, were placed in Warburg flasks and equilibrated at 37°C for 15 minutes before 0.5 ml of serotonin creatinine sulfate (6 μmole) was tipped in. The reaction was allowed to proceed in air for various intervals and was then stopped by the addition of 1 ml of 10 percent trichloroacetic acid. Spectra of suitably diluted filtrates were determined on the Beckman DU spectrophotometer.

The characteristic ultraviolet absorption of serotonin rapidly diminished, becoming eventually about half as intense as it was initially. In the visible region, a broad absorption band centered at about 530 mμ developed, but this was later obscured by more rapidly increasing absorption at shorter wave lengths. In this, as in other experiments with varying concentrations of enzyme and substrate, two atoms of oxygen per molecule of substrate were consumed. The shape of oxygen consumption and time-absorbance curves suggested that two consecutive oxidation steps might be occurring and that the second step gained no appreciable velocity until the first was essentially complete. Therefore, for mathematical analysis of the data, it was assumed that, during the earlier part of the oxidation, the only species present which absorbed visible light was the first oxidation product, P_1. Relating oxygen consumption to absorbance yielded extinction coefficients at two wavelengths for P_1. Here,

$$A_{400} = \varepsilon_{1\text{-}400}\, p_1$$

and

$$A_{530} = \varepsilon_{1\text{-}530}\, p_1$$

where A is absorbance, $\varepsilon_{1\text{-}400}$ and $\varepsilon_{1\text{-}530}$ are extinction coefficients at $\lambda = 400$ mμ and 530 mμ, respectively, and p_1 is observed oxygen consumption in microliters.

At completion, when only the second product P_2 was presumably present, oxygen consumption was related to absorbance to obtain extinction coefficients for P_2. In this case

$$A_{400} = \varepsilon_{2\text{-}400}\, p_2'$$

and

$$A_{530} = \varepsilon_{2\text{-}530}\, p_2'$$

where p_2' is one-half of the observed oxygen consumption at completion of the reaction and is equal to one atom of oxygen per molecule of serotonin originally present.

At any time during the oxidation

$$A_{400} = \varepsilon_{1\text{-}400}\, p_1 + \varepsilon_{2\text{-}400}\, p_2$$

and

$$A_{530} = \varepsilon_{1\text{-}530}\, p_1 + \varepsilon_{2\text{-}530}\, p_2$$

Simultaneous solution of these equations gave values for p_1 and p_2 in terms of microliters of oxygen absorbed; these values are plotted against time in Fig. 1. Total oxygen consumed up to any time would equal the amount of P_1 present (p_1) plus twice the amount of P_2 present ($2p_2$) at that time. This sum yielded the calculated oxygen consumption curve in Fig. 1, which fits the observed values well.

By varying the ratio of enzyme to substrate, it was possible to estimate the velocity constant and Michaelis' constant for the first reaction. From the rate of appearance of P_2 shown in Fig. 1, these constants for the second reaction were calculated. In this way it was found that the first reaction was about twice as rapid as the second and that the affinity of the enzyme for serotonin was some 3.6 times as great as it was for the first oxidation product. Since Michaelis' constant is not identical with the association constant, this latter figure is at best a rough estimate of the true ratio of affinities.

Ceruloplasmin has no monoamine oxidase activity. Neither does it catalyze the oxidation of monoamine oxidase substrates such as tyramine and phenethylamine, nor does it liberate ammonia in the course of the catalyzed oxidation of serotonin.

Like serotonin, 2-methylserotonin absorbed 2 atoms of oxygen per molecule, which indicates that the 2-position is probably not a point of oxidative attack. Polymerization of oxidized serotonin to melaninlike pigments is not likely in view of the report (*5*) that only benzene-oxygenated indoles which are unsubstituted in position 3 react in this way.

The oxidation of serotonin exhibits certain similarities to the tyrosinase-catalyzed oxidation of catechol (*6*), where oxidation to *o*-quinone is followed by hydroxylation. The two reactions differ in several respects, one being that in the tyrosinase-catechol reaction, more than two oxygen atoms can be consumed, depending upon the ratio of enzyme to substrate (*7*).

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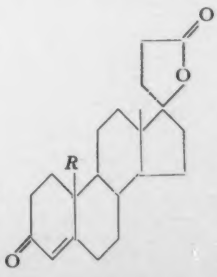
26 June 1957

Action of New Steroids in Blocking Effects of Aldosterone and Deoxycorticosterone on Salt

Aldosterone may be of etiological significance in salt and water retention of congestive heart failure, nephrosis, liver cirrhosis, and toxemia of pregnancy (*1*). We wish to report aldosterone-blocking activity of 3-(3-oxo-17β-hydroxy-4-androsten-17α-yl)propionic acid γ-lactone (SC-5233) and its 19-nor analog (SC-8109 (*2*). Such compounds may serve as useful agents in elucidating the role of aldosterone in edema and may be of value in the treatment of edema. Structures of the steroids are as follows:



In steroid SC-5233, R is CH_3; in steroid SC-8109, R is H. Results demonstrating aldosterone-blocking activity with SC-5233 are summarized in Fig. 1. Aldosterone in a solution of ethanol in 0.86-percent sodium chloride (20/80 by volume) was subcutaneously injected into adrenalectomized rats, either alone or with oil solutions of SC-5233. Four-hour samples of urine were collected from individual animals for sodium and potassium analyses. Aldosterone alone caused a reduction in the value of the Na/K ratio in the urine, but in the presence of 1.2 and 4.8 mg of SC-5233 per rat this reduction was significantly reversed.

The 19-nor analog, SC-8109, similarly blocked aldosterone activity. For example, administration of 0.98 μg of aldosterone reduced the Na/K ratio to 0.63 ± 0.07 (mean ± standard error). A dose of 1.3 mg of SC-8109 significantly counteracted this effect, giving a ratio of 1.12 ± 0.12. We attach strong importance to these findings because SC-5233 and SC-8109 appear to represent the first known examples of aldosterone blockers.

Several studies were undertaken to define the mechanism of blocking with deoxycorticosterone acetate (DOCA). We used this compound because of its availability, structure, electrolytic effects, and possible similarity in mechanism of action to aldosterone. The results obtained with DOCA and SC-5233 are summarized in the succeeding paragraphs; those obtained with SC-8109 are incomplete (*3, 4*).

A progressive blocking of the action of 12 μg of DOCA on the Na/K ratio was obtained with six different doses of SC-5233, ranging from 0.15 to 4.8 mg. These data showed that approximately 0.24 mg of SC-5233 was required for a 50-percent block of DOCA (*5*). Progesterone, which was recently described as a DOCA-blocker in man (*6*), showed similar activity with a dose of 1.8 mg. Compound SC-8109 was effective at 0.067 mg. By comparison of doses, progesterone, SC-5233, and SC-8109 showed relative activities of 1, 7.5, and 26.8, respectively.

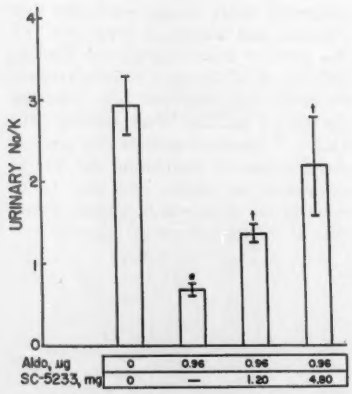


Fig. 1. Effects of SC-5233 in blocking urinary Na/K action of aldosterone in adrenalectomized rats (12 animals per treatment). Standard error is shown by vertical lines. * $P < 0.05$, compared with no treatment; † $P < 0.05$, compared with treatment with aldosterone alone.

Table 1. Effects of various doses of SC-5233 in blocking the action of deoxycorticosterone acetate (DOCA) in adrenalectomized rats.

Treatment (dose per rat)		No. of rats	Urinary Na/K (mean ± S.E.*)
SC-5233 (mg)	DOCA (μg)		
	24	20	0.47 ± 0.04
	48	19	0.54 ± 0.05
0.6	24	9	0.80 ± 0.13
1.2	48	9	0.81 ± 0.04
2.4	24	9	1.35 ± 0.36
4.8	48	9	1.23 ± 0.15
9.6	24	9	1.54 ± 0.40
19.2	48	8	1.62 ± 0.19

* S.E. = standard error.

Table 2. Effects of large amounts of deoxycorticosterone acetate (DOCA) in overcoming blocking action of SC-5233 in adrenalectomized rats.

Treatment (dose per rat)		Urinary Na/K (mean ± S.E.*)
SC-5233 (mg)	DOCA (μg)	
2.4	48	1.09 ± 0.13
2.4	240	0.75 ± 0.13
2.4	1200	0.69 ± 0.16
	48	0.54 ± 0.10

* S.E. = standard error; 15 rats per treatment; 20 untreated controls showed a Na/K response of 1.90.

The effects of SC-5233 in counteracting reduction of the Na/K ratio produced by 24 and 48 μg of DOCA were investigated at two dosage levels and at various ratios (Table 1). Doubling the dose at a fixed ratio of SC-5233/DOCA did not cause significant changes in Na/K values. Increasing ratios of SC-5233/DOCA, however, progressively blocked the effects of 24 and 48 μg of DOCA. These observations suggest that (i) equal blocking results with similar ratios and (ii) blocking increases with larger ratios of SC-5233/DOCA. It would appear that SC-5233 acts as a blocker according to the law of mass action.

The opposite question of reversing the action of SC-5233 with an excess of DOCA was studied (Table 2). The results indicate that the effects of 2.4 mg of SC-5233 were reversed with 240 and 1200 μg of DOCA. We feel that these results demonstrate reversible competition.

In order to rule out the possibility that SC-5233 had a direct effect of increasing the urinary Na/K ratio, instead of specifically blocking DOCA, we performed the following experiment. Doses of 0.0, 1.2, 9.6, and 19.2 mg of SC-5233 alone were given; these doses produced Na/K ratios of 2.15, 2.38, 2.67, and 2.32, respectively (nine rats per treatment). None of the responses with SC-5233 treatment significantly exceeded the control response of 2.15. Increases in the Na/K ratio greater than 0.66 above the control value would occur by chance once in ten trials, whereas in our results the largest increase was 0.52. Thus, SC-5233 does not in itself greatly affect the urinary Na/K ratio.

The results of these studies strongly suggest that SC-5233 and, possibly, SC-8109 exert their effects on electrolytes by competition with DOCA and aldosterone (*7*).

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3. A more detailed report on these investigations and other pharmacological effects of SC-5233 and SC-8109 is in preparation.
4. When given orally, 4.8 mg of SC-8109 significantly reversed the Na/K effect of 12 μg of DOCA from 0.59 ± 0.05 (mean ± standard error) to 0.95 ± 0.14. At the same oral dose, SC-5233 was inactive.
5. The term *percent block* refers to values obtained by the following formula: (net blocking effect of test compound) × 100/(effect of DOCA).
6. R. L. Landau *et al.*, *J. Clin. Endocrinol. and Metabolism* 15, 1194 (1955); R. L. Landau *et al.*, report presented at the meeting of the Endocrine Society, Chicago, Ill., June 1956.
7. We gratefully acknowledge the valuable technical assistance of Marjorie A. Thomas and Elizabeth D. Griffin. Thanks are due to David W. Calhoun for the statistical work.

30 July 1957

Sodium Diuresis Induced by Steroidal Antagonists of Aldosterone

For several years it has been known that the adrenal cortex secretes a number of steroidal hormones which increase the tendency of the renal tubules to reabsorb sodium. The adrenal steroid of most importance in the physiological regulation of electrolyte metabolism is aldosterone (*1*). Aldosterone has been shown to play a crucial role in normal physiology in promoting the conservation

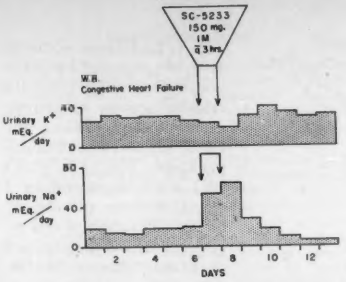

Fig. 1. Effect of SC-5233 on potassium and sodium excretion in a patient with congestive heart failure. Diet was constant from day to day.

of sodium in the face of sodium deprivation. It has also been implicated in the pathogenesis of the abnormal sodium and water accumulation which occurs in the "edematous states," such as congestive heart failure. There has been considerable interest in the possibility that the adrenal cortex may also elaborate a "sodium-losing" hormone (*2*). Identification of such a hormone has not yet been accomplished.

The present report (*3*) submits evidence that certain *synthetic* steroids, 3-(3-oxo-17β-hydroxy-4-androsten-17α-yl)-propionic acid γ-lactone (SC-5233) and its 19-nor analog (SC-8109) can act as natriuretic agents. The evidence strongly suggests that the mechanism of action of the new sodium-losing steroids is that of antagonism of the sodium-retaining action of aldosterone. Because of its earlier availability, SC-5233 was employed in the majority of these experiments. Compound SC-8109 has activity qualitatively like that of SC-5233, and it appears to be effective in smaller doses than SC-5233.

Preliminary studies with adrenalectomized dogs indicated that SC-5233, when administered alone, had no appreciable effect on electrolyte excretion. As previously reported (*4*), deoxycorticosterone (DOC), like aldosterone, regularly induces sodium retention and potassium excretion when it is administered to adrenalectomized dogs. The administration of CS-5233 together with deoxycorticosterone diminished the effectiveness of the latter with respect to both sodium conservation and potassium loss. The degree of attenuation of the effectiveness of DOC was a direct function of the dose of SC-5233 and an inverse function of the dose of DOC employed. These laboratory results confirm those obtained by Kagawa *et al.* with adrenalectomized rats (*5*). It is important to observe that the inhibitory action of SC-5233 is not limited to the sodium-retaining action of DOC but affects also the potassium-losing action of DOC. Numerous compounds (including cortisone) will cause an acute rise in sodium excretion in adrenalectomized dogs and rats. Of the compounds studied thus far, only SC-5233 and SC-8109 have been found to cause a simultaneous *inhibition* of potassium excretion. This change in the qualitative pattern of the electrolytic composition of the urine suggests that the site of action of SC-5233 is the renal tubule.

Metabolic studies in man clearly indicated that SC-5233 is an effective antagonist of aldosterone. In the absence of sodium-retaining steroids, SC-5233 had little or no effect. However, in the presence of sodium-retaining steroids, SC-5233 exhibited its characteristic natriuretic (without kaliuretic) action. This was demonstrated in three situations.

1) In seven patients with varying degrees of edema (due to congestive heart failure or nephrosis) the administration of SC-5233 consistently induced natriuresis (Fig. 1).

2) A patient with negligible adrenal function due to Addison's disease was given SC-5233 while being maintained on a high sodium diet without steroids. SC-5233 failed to induce a convincing change in electrolyte excretion (Fig. 2). When the same patient was maintained on a high sodium diet plus DOCA, the addition of SC-5233 induced a rise in sodium excretion. Potassium excretion not only failed to rise but actually showed a slight fall.

3) Normal subjects receiving a high sodium intake were treated with SC-5233 with no significant effect. (It has been shown repeatedly in the past and was found again in the course of this study that normal subjects on high sodium intake have minimal levels of aldosterone.) The same normal subjects, while receiving a low sodium intake, were again treated with SC-5233; under these circumstances SC-5233 induced an increase in urinary sodium. (As in previous studies, aldosterone was found in the urine in relatively large amounts during the course of the low sodium diet.)

The conclusion appears secure that SC-5233 is effective as a natriuretic agent only in the presence of sodium-retaining

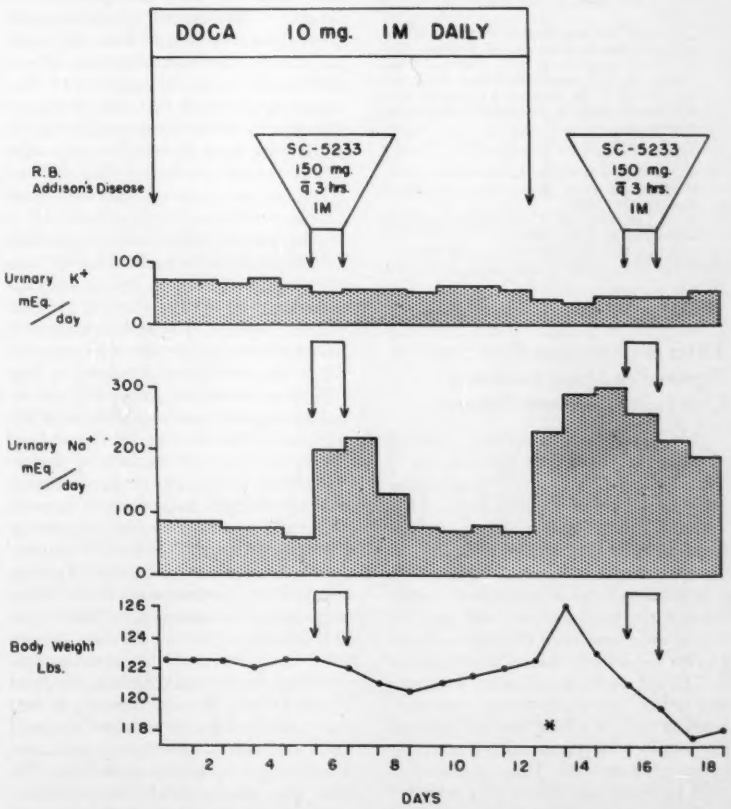

Fig. 2. Effect of SC-5233 on potassium and sodium excretion in a patient with Addison's disease. Diet was constant from day to day. Deoxycorticosterone acetate in sesame oil was injected intramuscularly in doses of 5 mg every 12 hours during the first 12 days. On day 13 (marked by an asterisk) the sodium deficit resulting from the initial treatment with SC-5233 was repaired by ingestion of 18 g of NaCl. SC-5233 was administered intramuscularly in doses of 150 mg (in 3 ml of sesame oil) every 3 hours for 8 doses on day 6 and day 16.

steroids, endogenous or exogenous. The most reasonable interpretation of these findings is that SC-5233 and, presumably, SC-8109 act as antagonists to aldosterone and other sodium-retaining steroids. It is suggested that the mechanism through which these sodium-losing steroids act is that of competition with aldosteronelike steroids for a crucial locus of action within the renal tubular cells. A similar mechanism has been postulated previously to explain the sodium loss which has occasionally been seen during treatment of patients with supraphysiologic amounts of cortisone (*6*) and progesterone (*7*).

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3. This study was supported in part by grants-in-aid from the National Cancer Institute (CY-3107) and from the John A. Hartford Foundation. SC-5233 and SC-8109 were generously provided by G. D. Searle and Company. Donald Island rendered invaluable technical assistance.
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19 August 1957

Effect of Citrovorum Factor and Peptones on Mouse Leukemia Cells L-5178 in Tissue Culture

A medium has been devised (*1*) which permits the continuous reproduction of mouse leukemia cells (L-5178, a lymphocytic neoplasm of DBA/2 mice, *2*) in culture in the complete absence of nonleukemic cells (*3*). After at least 150 successive generations *in vitro*, the cells have continued to grow in suspension (rather than on the glass surface), and have retained their round-cell character, as well as their capacity to induce fatal leukemia in DBA/2 mice. In addition to serum and other ingredients usually encountered in culture media, certain peptones are required for the continued multiplication of these cells. Data presented in 1928 by Baker and Carrel and extended by Willmer and Kendal (*4*) indicated that various peptones can stimulate the multiplication of mammalian and avian cells in tissue culture. More recently, Waymouth has reported that peptone, in the presence of albumin, replaces serum for the multiplication of strain L mouse cells (*5*). However, the factors in peptone which support cell multiplication have not been identified. Previous studies of the growth responses of *Lactobacillus leichmannii* (ATCC 7830) and *Pedicoccus cerevisiae* [*Leuconostoc citrovorum* (ATCC 8081)] to peptonelike materials and the relationship of the responses to vitamin B_{12}, citrovorum factor, and thymidine have been described (*6, 7*).

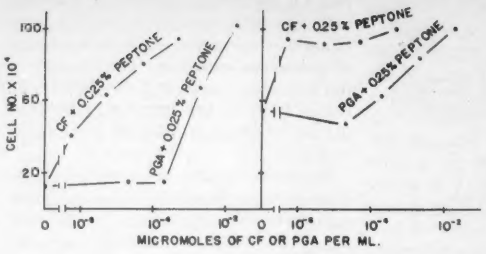

Fig. 1. Reduction of the effect of peptone by citrovorum factor (CF) and the relative activity of pteroylglutamic acid (PGA) and CF in support of cell multiplication. The cells (2.0×10^5) were incubated in 1 ml of medium (*1*) for 48 hours; the extent of cell reproduction was determined by hemocytometer counts.

Experiments (*8*) directed toward the isolation of the active factors in the peptone used (*9*) have demonstrated that synthetic 5-formyl-5,6,7,8-tetrahydropteroylglutamic acid (citrovorum factor; CF; folinic acid; leucovorin) partially replaces peptone in the nutrition of these leukemic cells and that the capacity of the cells to obtain functional derivatives from folic acid (pteroylglutamic acid; PGA) is very much less than their capacity to obtain them from citrovorum factor.

The partial replacement of peptone by leucovorin in the nutrition of the neoplastic cells is shown in Fig. 1. The data indicate that, in the presence of 0.025 percent peptone, a stimulatory effect of leucovorin was clearly demonstrable, while at a ten-fold higher level of peptone, very much less leucovorin was required to attain maximal growth. In this 48-hour experiment, at the lower level of peptone, 3.7×10^{-6} μmole of the active form of leucovorin per milliliter (*10*) permitted half-maximal growth, while a 400-fold higher concentration of pteroylglutamic acid (1.5×10^{-3} μmole/ml) was required to obtain a similar effect. When cultures were carried for a minimum of ten progressive generations, in triplicate, on limiting levels of the two coenzyme-precursors, the doubling-time was less than maximal and remained constant, and, in addition, equivalent rates of multiplication were obtained with active leucovorin in a concentration 1/5000 that of pteroylglutamic acid. The fact that the doubling-time remained constant indicates that, in the presence of either pteridine derivative, certain components of the peptone are no longer required for the nutrition of the cells. During continuous culture in media containing a much higher level of peptone, 0.5 percent, but only 2.2×10^{-5} μmole of pteroylglutamic acid per milliliter, a generation time of less than 22 hours (average, 24 hours) was rarely obtained. In contrast, generation times of 14 to 22 hours (average, 18 hours) were obtained with optimal amounts of active leucovorin (2×10^{-5} μmole/ml) or with very high levels of pteroylglutamic acid (2×10^{-2} μmole/ml) in the presence of low levels of peptone (0.06 percent).

The high levels of folic acid, as compared with the levels of its tetrahydro derivative, which are required to support cell multiplication indicate a very limited capacity of the leukemic cells under these conditions to synthesize coenzymes from pteroylglutamic acid (*11*). The absolute requirement of certain other cell lines for this vitamin is very much less than it is for L-5178, for example, HeLa and L-strain (*12*), a finding which suggests that these cells efficiently convert folic acid to coenzyme forms. Such an interpretation is supported by the fact that citrovorum factor is only 20 to 30 times as effective as pteroylglutamic acid for L-strain cells (*13*). Although the requirement for folic acid of sarcoma 180 cells in tissue culture resembles that of both L-strain and HeLa cells, our colleague, Richard Schindler, has found that this requirement is met (in Eagle's medium, *12*) by active leucovorin in an amount approximately 1/200 that of pteroylglutamic acid.

It is well known that various neoplastic cell lines, *in vivo*, exhibit widely variable sensitivity to the chemotherapeutic action of A-methopterin, an agent which inhibits the enzymic conversion of folic acid to tetrahydro derivatives. It is suggested that the effectiveness of A-methopterin as an inhibitor of the reproduction of various types of cells is markedly influenced not only by the extracellular supply of tetrahydro derivatives of folic acid, but also by the enzymic capacity of such cells to convert folic acid-like compounds to coenzymically active, tetrahydro forms (*14*).

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1. Each 100 ml of medium contained vitamins, glucose, cystine, histidine, and glycine at the levels employed by W. Scherrer [*Am. J. Pathol.* 29, 113 (1953)] and, in addition, acid-hydrolyzed casein (N. B. Co.) (25 mg), undialyzed horse serum (10 ml), peptone (60 mg), glutamine (15 mg), hypoxanthine (2.5 mg), tryptophan (0.25 mg), glutathione (0.15 mg), sodium ascorbate (0.175 mg), and, unless otherwise stated, pteroylglutamic acid (1 mg). Stock cultures were carried by daily transplantation of about 4×10^6 cells in 10 ml of the freshly prepared medium. Serum was dialyzed with stirring for 60 hours against nine changes, each of 10 volumes of distilled water.
2. Kindly supplied by Lloyd W. Law of the National Cancer Institute, Bethesda, Md.
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8. In collaboration with R. E. Handschumacher.
9. In most of these experiments, the peptone used was that supplied by the Walker Laboratories, to whom our thanks are due.
10. This calculation recognizes that only one enantiomorph of the racemic, synthetic citrovorum factor, that is, leucovorin (for the supply of which we are indebted to the Lederle Laboratories Division of the American Cyanamid Company), is available for biological utilization.
11. These results were not materially affected by the use of dialyzed horse serum at the 6-percent level in place of the 10-percent undialyzed horse serum of the basal medium. However, increasing the level of dialyzed or undialyzed serum promoted growth when either PGA or CF was limiting.
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14. A generous grant from the Jane Coffin Childs Memorial Fund for Cancer Research permitted the equipment of a laboratory for tissue culture studies and contributed to the costs of the research. This program was also contributed to by grants from the American Cancer Society and the U.S. Public Health Service. One of us (G.A.F.) is grateful for a special fellowship from a fund generously provided by the Squibb Institute for Medical Research.

25 July 1957

Self-Regulation of Protein Synthesis in Acetabularia

The regulation of normal and abnormal growth has recently attracted extensive studies in numerous areas. The interaction of intracellular growth-promoting substances and extracellular growth-inhibiting substances has been postulated (*1*). In the present study, we have concentrated on the intracellular regulation and limitation of protein synthesis.

We utilized a large unicellular alga, *Acetabularia crenulata* (*2*), cultured in sea water according to the method of Haemmerling (*3*). The unique size of the cell (3 to 4 cm) and nucleus (200 μ) allows an easy preparation of anuclear fragments of sizes varying from 0.5 to 40 mm. Because of the cylindrical shape of the stalks, these algae offer an excellent material for the investigation of the relationship between the rate of growth, as expressed by the rate of protein synthesis, and the relative surface (area/volume) of the cell.

Individual cells, measuring 21 to 23 mm in length, were enucleated by removal of rhizoids. Some of the resulting stalks, 19.3 ± 0.2 mm in length and 0.5 mm in diameter, were then analyzed for nitrogen by the method of Johnson (*4*) after the nonprotein nitrogen had been removed with 10-percent trichloroacetic acid. The average value of protein nitrogen was 4.8 μg per stalk with a variation of 0.2 μg as estimated from three samples, each of which consisted of 12 stalks. Other stalks were cut transversely, some in halves, others into quarters, and still others into eighths. Approximately 12 percent of the stalks partially lost their cytoplasm during cutting and were discarded. After 15 days, all fragments that had come from a single stalk were analyzed together for protein nitrogen. The amount of protein synthesized by each fragmented stalk was calculated from the difference between the protein nitrogen content of the fragmented stalks at the end of the 15-day period and that of the unsegmented stalks analyzed at the begining of the experiment. Fourteen samples were used for each value represented in Fig. 1. Variations among the samples were within 10 percent.

The surface area and volume of each stalk were calculated on the basis of the assumption that the stalk was cylindrical in shape. Since the stalk was cut transversely, the total surface area was increased only at the cut ends. The relative increase in surface area due to cutting was expressed as a percentage of the total surface area of the uncut stalk.

Figure 1 shows that the amount of protein synthesized during the 15-day period per stalk (total synthesis), as well as the amount of protein formed expressed as a percentage of the original protein content (relative synthesis), increases with the number of fragments into which the stalk has been cut. On the other hand, the relative increase in surface area due to cutting of stalks shows only a small rise as the number of fragments increases. These findings indicate that the increase in protein synthesis cannot be satisfactorily explained on the basis of a higher absorption rate of nutrients resulting from an increase in surface area after cutting.

To ascertain the influence of initial length and protein content of stalks on the rate of protein synthesis, 130 cells were cut at various distances from the growing tips of the stalks to provide anuclear fragments of various lengths, each of which contained one intact end and one cut end. Twenty of them were analyzed immediately for protein nitrogen, and the others were grown in the standard medium for 15 days. In this experiment the differences in surface area of stalks of different lengths are due to the size of the lateral walls. Thus, all stalks were subjected to a similar injury at the cut ends. The volume of each fragment varies directly as its length under these conditions. The difference in relative surface area is expressed as the excess of the area/volume ratio of any stalk above that of the longest (36 mm).

As can be seen in Fig. 2, the total protein synthesis per stalk, as well as the

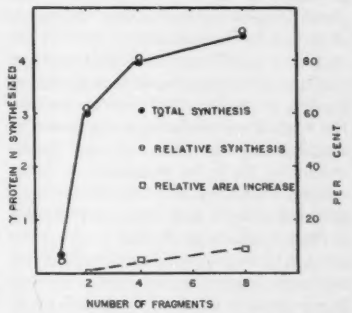

Fig. 1. Effect on protein synthesis of cutting anuclear stalks into a number of fragments. The ordinate to the left represents micrograms of protein nitrogen synthesized per stalk. The term *total synthesis* refers to the absolute value of protein N synthesized, while *relative synthesis* expresses the same value as a percentage of the original protein N content of the stalk. *Relative area increase* represents the increase of surface area due to cutting, expressed as a percentage of an unsegmented stalk.

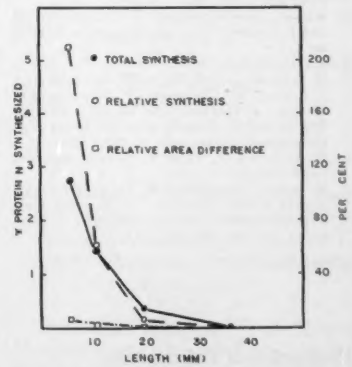

Fig. 2. Relationship between the length of anuclear stalks and the rate of protein synthesis. The ordinates are the same as those in Fig. 1. The term *relative area difference* refers to the excess of area/volume ratio of any stalk over that of the longest stalk (36 cm), expressed as a percentage of the latter.

relative protein synthesis, varies inversely as the length of the stalks at the beginning of the experiment. The difference in relative area, on the other hand, does not show any significant variation among stalks that differ greatly in length. This offers even more convincing evidence that an increase in surface area does not play a significant role in the higher rate of protein synthesis in the shorter stalks. Moreover, since all stalks have been subjected to a similar amount of injury, the operative procedure can be eliminated as a factor in the phenomenon.

These experiments are considered to reveal additional evidence of the independence of the cytoplasmic protein synthesis from the presence of a nucleus as described by Brachet and co-workers (*5*) and Stich and Plaut (*6*). The cytoplasm and not the nucleus must be regarded as playing an essential role in determining the amount of synthesized proteins. The simplest interpretation of our results would be made by assuming an intracellular inhibitory effect which increases with cell growth and which is reversible if the cytoplasm is divided into smaller units. The higher activity of smaller cytoplasmic fragments may explain the surprising results obtained by Brachet (*5*) and Beth (*7*) that cytoplasmic fragments synthesize proteins and differentiate at a faster rate if the nucleus containing rhizoid is removed.

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9 September 1957

Production of Tolerance to Psychosis-Producing Doses of Lysergic Acid Diethylamide

It has been shown that 2 mg of crude beef brain extract per milliliter blocks the usual effect of 2 μg of lysergic acid diethylamide (LSD-25) per milliliter in the outside liquid on the Siamese fighting fish (*1*). This report (*2*) describes a study of a blocking effect that is probably produced by another mechanism: the development of tolerance to LSD-25 in man (*3*) by the prior administration for a period of days of a compound similar to LSD-25, 1-methyl lysergic acid diethylamide (MLD-41) (*4*).

Table 1. Comparison of production of tolerance to lysergic acid diethylamide (LSD-25) by 1-methyl lysergic acid diethylamide (MLD-41) and 2-bromo lysergic acid diethylamide (BOL-148).

Date of experiment	Total preparatory dose of MLD-41 (μg)	Pretreatment period	Total preparatory dose of BOL-148 (μg)	LSD-25 (μg)	Responses (No.)
29 March 1957	0		0	50	35
12 April 1957	1100	7 to 12 April	0	80	0
10 May 1957	700	4 to 10 May	0	100	7
7 June 1957	0	1 to 7 June	1450	50	14
21 June 1957	0	16 to 21 June	1000	50	21

1-Methyl lysergic acid diethylamide produces in man and the Siamese fighting fish reactions that are essentially indistinguishable from those produced by LSD-25, but there are higher reaction thresholds. In the fish, MLD-41 is about one-tenth as effective as LSD-25; it is approximately one-third as effective in man, as judged by our questionnaire technique. The questionnaire consists of a first part containing 47 questions and a second part containing nine reactions, which are rated both by the subject and by the observer. Positive responses to the questionnaire are added irrespective of the intensity of the response. Thus, in Table 1 the total of positive responses to the questionnaire refers to the sum of both parts of this questionnaire (*5*).

The effect of MLD-41 on man was obtained by giving it to a group of five nonpsychotic test subjects who have been used in the study of LSD-25 and its derivatives for the past 3 years. Both LSD-25 and MLD-41 were administered orally in distilled water or tap water with no essential differences observed between the two. Development of tolerance to LSD-25 was achieved by administering MLD-41 for 5 or 6 days in increasing doses, starting with 100 μg on the first day and reaching 350 μg on the fifth day. Since the threshold to MLD-41 is approximately 70 μg orally, tolerance to MLD-41 itself was developed rapidly. It appears that approximately 1000 μg of MLD-41 administered in this way protects against approximately 80 to 100 μg of LSD-25 taken orally 8 hours after the last dose of MLD-41.

Table 1 illustrates a typical series of experiments on one of our subjects. Although 2-bromo lysergic acid diethylamide (BOL-148) produces some tolerance to LSD-25, its effect for equal weights is much less, approximately one-third of that of MLD-41. The highest doses of LSD-25 varied from 1.1 to 1.6 μg/kg of body weight. These doses invariably produced a severe typical LSD-25 reaction in our test group. Note in Table 1 that, whereas 50 μg of LSD-25 in this subject, without pretreatment by MLD-41, produces 35 positive responses to the questionnaire, there were no positive responses to the questionnaire following a 50 μg dose of LSD-25 when this subject had been pretreated for 5 days with 1100 μg of MLD-41.

A similar experiment in which BOL-148 was substituted for MLD-41 resulted in 21 positive responses to the questionnaire (21 June 1957). The 21 positive responses obtained represent the equivalent of at least a 25-μg response to the LSD-25 administered. The subject himself estimated that he experienced a 35-μg LSD response.

The fact that a substance like MLD-41, which is less toxic than LSD-25, can produce a marked tolerance to LSD-25 lends hope to the possibility that if the schizophrenias are produced by a disturbance in biochemical mechanisms analogous to that resulting from the administration of mescaline, LSD-25, and similar substances, there is good reason to believe that comparatively nontoxic molecules might be administered to produce a similar tolerance to the chemicals that originate the schizophrenic state.

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2. This investigation has been aided in part by grants from the Josiah Macy, Jr. Foundation, New York, N.Y., and the Foundation for Research in Pulmonary Disease, New York, N.Y.
3. H. A. Abramson *et al.*, *J. Psychol.* 41, 81 (1956).
4. We are indebted to Sandoz Pharmaceuticals for the supplies of MLD-41 and BOL-148.
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27 August 1957

Book Reviews

Semiconductors. Their Theory and Practice. G. Goudet and C. Meuleau. Translated by G. King from *Théorie et Pratique des Semiconducteurs* (Editions Eyrolles, Paris). MacDonald & Evans, London, 1957 (order from Essential Books, Fair Lawn, N.J.). xviii + 316 pp. $18.90.

The authors deal with the subject of semiconductors, from basic quantum mechanics through device technology, in one of the first attempts to do this since Shockley's book, *Electrons and Holes in Semiconductors* (Van Nostrand, 1950). Because of the many recent developments in the field of semiconductor technology, this is a welcome addition to the field.

The book is divided into three parts: "General Fundamental Theories"; "The Technology of Semiconductors"; and "The Principal Applications of Semiconductors, Thermistors, and Varistors." The first part gives a concise but clear development of the elements of quantum mechanics, applying the analogy of geometrical and physical optics to classical and quantum mechanics. The band theory of solids is treated in both one and two dimensions, and the Fermi-Dirac statistics are derived as well as discussed. Part 1 concludes with a section on electric current in solids, which includes transition probabilities, conductivity, and the Hall coefficient. All of this occupies only 126 pages but, despite its brevity, the book should provide a useful introduction to the theory of solids, particularly for engineers.

In part 2 the general properties of crystals are discussed. The intermetallic compounds are reviewed, as well as germanium and silicon. A chapter is devoted to the techniques of preparing high-purity crystals, including zone refining and pulling techniques. Another chapter describes measurements used in production and research. Part 2 occupies only 60 pages, but the brief descriptions are clear and, with some 184 references, should be quite useful to both engineers and physicists.

Part 3 discusses semiconductor devices in four chapters, on thermistors and varistors, diodes and rectifiers, crystal triodes and tetrodes, and other devices (photoconductive cells, radioactive batteries, magnetometers, and so on). The basic transistor equations are derived, and equivalent circuits are given. While all of this is done in the short space of 116 pages, the treatments are quite adequate, and a bibliography of 137 papers serves to round out the work.

The authors are to be congratulated; the book provides an excellent introduction to semiconductor physics and technology and should be of use to engineers and physicists, both as an introductory text and as a reference work.

RICHARD L. PETRITZ
U.S. Naval Ordnance Laboratory

Excited States in Chemistry and Biology. C. Reid. Academic Press, New York; Butterworths, London, 1957. ix + 215 pp. Illus. $7.50.

"As any area of inquiry develops into exact science it passes through a succession of stages which may be roughly designated Macroscopic, Microscopic, Molecular and Submolecular." This has been fully recognized by chemists who want to have a deeper insight into the mechanism and nature of chemical reactions. Biology is just on the verge of this new development, and the intention of the author is to give a helping hand to both chemists and biologists by outlining "some of the more important physical concepts concerning molecular excitation and interaction." This he does very successfully within a small booklet, which does not overwhelm the reader by its volume and technicality.

Essentially, the book consists of three parts: an outline of quantum mechanics, the discussion of selected biological problems, and an appendix in which the author discusses a few problems of quantum mechanics in more detail.

The first 50 pages are devoted to the mathematical foundations of quantum mechanics, and remain intelligible all the way through, to the well-informed general reader. Then follows the discussion of spectra, excitation mechanisms, and the triplet state, to which latter the author evidently attributes first-rate importance for the understanding of chemical and biological processes. After treating the various mechanisms of inter- and intramolecular energy exchange, the author discusses biological luminescence, vision, and the biological effects of high-energy radiation from the point of view of quantum mechanics. Being a biologist, I cannot help being impressed by the vastness of the field covered and the extent of the underlying information. The physics presented must be of at least equal quality, the author being a physicist and not a biologist.

The appendix deals with the Hamiltonian group theory, the theory of time-dependent perturbations, long-range energy transfer, and transition probabilities. The treatment of group theory is especially welcome, this theory being rather useful in its application and difficult to find in so short and clear a presentation. It is a sound plan to have these subjects covered in an appendix instead of having them break the continuity and reduce the palatability of the main chapters.

The treatment is clear, the outlay simple and transparent. If there is anything to regret, it is that the author did not dwell longer on certain topics and, for instance, give more of a qualitative and symbolistic interpretation of his quantum mechanics. A more detailed treatment of various kinds of spectra might have been useful. The reader should not allow himself to be discouraged by minor shortcomings, such as the sudden appearance of a mathematical symbol which is not explained and which finds no application later or the occasional reference to a wrong equation. Few books are exempt from such minor shortcomings; they detract but little from the value of the service the author has rendered to biologists and chemists by writing this book, lending them a helping hand in their attempt to apply quantum mechanics to their problems.

ALBERT SZENT-GYÖRGYI
Institute for Muscle Research, Marine Biological Laboratory

Mathematics for Everyman. From Simple Numbers to the Calculus. Egmont Colerus. Translated by B. C. and H. F. Brookes. Emerson, New York, 1957. xi + 255 pp. Illus. $3.95.

This book, subtitled "From Simple Numbers to the Calculus," is a popular introduction to mathematics in which the translators have succeeded in conveying "the spirit and enthusiasm of the original German." It covers, in a more or less descriptive way, elementary algebra, trigonometry, coordinate geometry, and calculus. This is done largely with heuristic arguments rather than exact proofs; for example, "We will not dally at this

point but present the necessary formula without further ado." Similarly, the definitions are not always very precise, as the author recognizes: "It is not our intention to confuse the reader with a series of definitions. That would be the usual textbook approach."

The result is a book that is very easy to read, but unfortunately this ease is partly obtained by glossing over the subtle and difficult points, especially in the calculus. The author realizes this to some degree, for he writes (page 175), "The expert in pure mathematics will probably hold up his hands in horror at our exposition. We believe however that it is better to have a rough idea than no idea at all. In any case our method was good enough to satisfy the mathematicians of the seventeenth century and any enthusiastic reader who wishes can pursue the subject further in a more comprehensive book of higher mathematics." How true! But the mathematician, whether he is in pure or applied mathematics, may be excused for balking at the antiquated treatment of the calculus or at such statements as (page 57): "Zero is not in itself a number though it is often treated as if it were; it separates the positive from the negative numbers."

It is a pity that the mathematics is not more accurate and up to date because there can be no question of the author's skill at exposition. His writing is lucid and entertaining, and it seems certain that many people in no position to recognize the inadequacies will find in the book just the thing they had been looking for in mathematics—an easy style, a constant encouragement to continue, and an absence of problems or exercises.

IVAN NIVEN

University of Oregon

Essays in Linguistics. Viking Fund Publications in Anthropology, No. 24. Joseph Greenberg. Wenner-Gren Foundation for Anthropological Research, New York, 1957 (order from University of Chicago Press). 108 pp. $3.

This collection of essays will further the increasing awareness of the significance of so fundamental a trait as language to any general science of human behavior.

The first two essays, on "Language as a Sign System" (pages 1–17) and "The Definition of Linguistic Units" (pages 18–34), are the most immediately relevant to general linguistic methodology. Of particular interest is the discussion of the nature of the grammatical analysis of natural languages and of how, given samples of expressions in the system, the linguist attempts to produce an infinite number of additional expressions which belong to the same system. By definition, an infinite number of expressions cannot be listed and, consequently, can only be generated by some set of rules. Current research in syntactic analysis is aimed at clarifying the techniques for deriving such rules and for identifying the units to which the rules apply. In this connection, most linguists will not agree with Greenberg's segmentation of forms like *man* into /m-n/ and /-æ-/ for the singular; rather they would prefer the analysis to reveal the similarity of the singulars *man* and *pan*; Greenberg's suggestion projects onto the singular forms the differences which are apparent in the corresponding plurals, *men* and *pans*. And, indeed, this is Greenberg's purpose: to make explicit the premises on which linguistic analysis is based and to develop the consequences of a rigorous adherence to those premises.

The essays on "Genetic Relationship among Languages" (pages 35–45) and "The Problem of Linguistic Subgroupings" (pages 46–55) contribute to a clarification of the assumptions of historical and comparative linguistics. It has sometimes been maintained that the comparative method involves a fundamental circularity—namely, that one cannot establish phonetic laws without cognates but that one cannot establish cognates without phonetic laws. Greenberg indicates four causes of sound-meaning similarities which may be observed between languages. Of these, two are nonhistorical—chance and symbolism, the latter being Greenberg's cover term for the occasional nonarbitrary connection between sound and meaning as exemplified by onomatopoetic forms and by some nursery words like those for "mother" and "father." "The remaining two—genetic relationship and borrowing—involve historic processes. The two basic methodologic processes then become the elimination of chance and symbolism leading to hypotheses of historic connections and the segregation of those instances in which borrowing is an adequate explanation from those on which genetic relationship must be posited" (page 37). Essentially, the circularity disappears with the establishment of other-than-chance resemblances.

The remaining four essays include a number of original and fruitful notions on such topics as language and evolutionary theory, genetic and nongenetic classifications, function, efficiency and redundancy in language, linguistic universals, and so forth.

The essays in this volume are independent of one another and are in no way intended as a systematic over-all treatment of linguistics. Nevertheless they seem to share two features: a desire to explore the relationship between linguistics and other disciplines—particularly logic, mathematics, anthropology, and psychology—and, in the process, to apply some of the more rigorous techniques developed in these areas to the scientific study of language. The result is a stimulating book, revealing a variety of approaches for the analysis of linguistic phenomena.

SOL SAPORTA

Indiana University

Meat Hygiene. WHO Monograph Series No. 33. World Health Organization, Geneva, 1957 (order from Columbia University Press, New York). 511 pp. Illus. $10.

In this book on meat hygiene, the World Health Organization has compiled papers prepared by 16 of the world's foremost authorities on the subject. The book is interesting, instructive, and beautifully illustrated.

Three of the papers are scientific treatises: those by C. E. Dolman, of the University of British Columbia, on meat-borne diseases; by H. Drieux (Ecole Nationale Veterinaire, Alfort, France), on tuberculosis; and by G. Schmid (University of Berne, Switzerland), on parasites.

The highly authenticated and well-documented papers of Dolman and Drieux highlight the monograph. In his "Epidemiology of Meat-Borne Diseases," Dolman organizes the material in a way that permits a full, convincing and logical presentation. He brings together the many ramifications of the subject of meat-borne diseases in a way that enables the reader to understand the relationship between the many probabilities that tend to confuse the student and even the meat-hygiene practitioner.

Drieux's paper on tuberculosis is a masterpiece. What is remarkable about his paper is that he has taken a subject that many would regard as having been pretty well exhausted by an array of authors and has given it fresh treatment from the meat hygienist's point of view. His paper serves two purposes—the first, of course, to inform the reader fully on the subject matter and the second—which seems to me to be more important—to inform meat hygienists that the science of disease evaluation in terms of fitness for food of an animal carcass is a fascinating and exacting one.

M. M. Kaplan (World Health Organization, Geneva) has a paper on meat-hygiene problems in tropical areas. His account of what might be described as primitive conditions as he sees them from the point of view of a public health official shows how the official's problem is complicated by merging of hygienic, eco-

nomic, and social factors. Kaplan's paper demonstrates the fundamental nature of the relationship of these three factors to the subject of meat hygiene. As is brought out in the other papers of the monograph, the hygienic, economic, and social factors all exert a profound influence on what might be referred to as the European meat-hygiene story.

The remaining papers sparkle with history, narrative, and philosophy concerning European practices and programs relating to the handling of food animals, their slaughter, and the preparation and handling of meat products. Papers by R. I. Hood and H. H. Johansen of the World Health Organization Regional Office for Europe describe, in detail, European meat-hygiene practices.

A paper by M. J. J. Houthuis (director, Municipal Slaughterhouse, Rotterdam, Netherlands) emphasizes the importance of ante-mortem inspection as the first step in the proper processing of food animals through a meat-packing plant.

Very informative papers on stunning methods are given by T. Blom (department chief, Royal Veterinary Board, Stockholm, Sweden) and Phyllis G. Croft (biochemist, Mile End Hospital, London). Electrical stunning, a subject now receiving considerable attention, is covered in detail.

Municipal abattoirs are discussed by G. Scaccia Scarafoni, (Istituto Superiore di Sanita, Rome) and Roger Benoit (director of abattoirs, Lausanne, Switzerland). These papers contain a very interesting discussion of the history of the development of municipal abattoirs in Europe and of the problems connected with their adjustment to present-day needs and standards.

H. Thornton (chief veterinary officer, City and County of Newcastle-upon-Tyne, England), who is a recognized authority in the field of applied meat-hygiene practices, emphasizes the importance of meat-hygiene programs being in the hands of properly trained and experienced inspectors, functioning methodically.

A paper by A. Jepsen (Royal Veterinary and Agricultural College, Copenhagen) is a real contribution to the monograph. In his lucid style, Jepsen points out the importance of inspectors having available adequate laboratory services. At the same time he cautions that the laboratory cannot be substituted for the inspector. He calls for the closest possible coordination and cooperation between the laboratory and field staff.

The World Health Organization is fortunate in being able to include in its monograph a paper by a man of the stature of F. Schönberg (Tierarztliche Hochschule, Hanover, Germany). He draws attention to the controls that must follow the meat as it leaves the slaughtering department and pursues its somewhat tortuous route to the consumer.

Worthy of special mention is the paper by S. O. Koch (chief veterinary officer, City of Aarhus, Denmark). Koch develops the subject of local control, which is frequently the weak link in the total meat-hygiene program. He not only writes convincingly on the subject of hygienic controls applied locally but he also heads up, in the city of Aarhus, a program that effectively applies the principles he describes.

The paper by V. E. Albertsen (chief veterinary inspector, Danish Veterinary Service, Copenhagen) deals with the subject of disposal of by-products. His paper gives emphasis to what has been mentioned incidentally in other papers—that the official functioning in an effective meat-hygiene program must be prepared to discharge responsibilities that cover a wide range of subject matter.

The monograph is complete, with an array of references, an appendix consisting of 146 pages, and a selected bibliography on meat hygiene.

A. R. MILLER
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U.S. Department of Agriculture

Advances in Enzymology and Related Subjects of Biochemistry. vol. 18. F. F. Nord, Ed. Interscience, New York, 1957. v + 435 pp. Illus. $9.

The 1957 volume of *Advances in Enzymology* lives up to the very high standards established over a period of 18 years. The present volume includes review articles by nine different authorities in various fields of enzymology and related subjects and will be of great value to chemists, biologists, and medical research workers as well as to biochemists.

In his review of cytochrome in higher plants, Hartree has pointed out the similarity of the cytochrome system of plants to that of animals, at the same time pointing out minor differences peculiar to plant systems.

Singer, Keaney, and Massey have reviewed the complex and controversial literature on succinic dehydrogenase and have related its function to electron carriers of the cell. They have also discussed the stepwise purification of succinic dehydrogenase from mitochondrial preparations.

Sir Rudolph Peters, in a review of the mechanism of toxicity of an active constituent of *Dichapetalum cymosum,* has shown that the toxic component is fluoroacetate, which in the animal organism undergoes a lethal synthesis to fluorocitrate, As a specific inhibitor of aconitase, fluorocitrate interferes with animal respiration by blocking the citric acid cycle.

The purification and properties of deoxyribonucleoprotein have been reviewed by Butler and Davison. In addition, these authors have briefly discussed its function in heredity and in protein biosynthesis.

Arthur Kornberg has surveyed the role of pyrophosphorylases and phosphorylases in biosynthetic reactions. In this outstanding review, a vast amount of diverse and apparently unrelated material has been correlated for the first time.

Wiame, in his review of the tricarboxylic acid cycle in microorganisms, has shown that this cycle is not only important in respiration but is also involved in the synthesis of many important biochemical compounds in bacteria.

James has reviewed the reaction patterns in the respiration of the higher plants and has shown the basic similarity of these pathways to those typical of animals. It is unfortunate that the role of cytochrome in higher plants, discussed by Hartree, is repeated in this article by James.

Reed has reviewed all of the literature on the chemistry and function of lipoic acid and has indicated certain enzymatic systems in which lipoic acid plays a role in living organisms.

In the final article, Schubert and Nord have examined the scattered and fragmentary literature on lignification and have considered the biosynthesis of lignin from vanillin, syringaldehyde, and *p*-hydroxybenzaldehyde, which are derived from shikimic acid.

With the number of enzyme systems now approaching 1000, it is unfortunate that an annual review can consider so few. In order to cover a wider diversity of enzyme systems, it would seem wiser to revert to the original pattern of the early volumes of *Advances of Enzymology,* in which reviews were only 20, instead of 42, pages in length. This would have the added advantage that the nonspecialist would not be plagued by the reading of so much unimportant detail.

IRWIN W. SIZER
Massachusetts Institute of Technology

Heat Transfer and Fluid Mechanics Institute, 1957. Preprints of papers. Held at California Institute of Technology, Pasadena, California, June 19–21, 1957. Stanford University Press, Stanford, Calif., 1957. vii + 439 pp. Illus. $8.50.

This publication contains 21 papers, in the areas of heat transfer and fluid mechanics, presented at the tenth meeting of the Heat Transfer and Fluid Mechanics Institute at California Institute of

Technology, 19–21 June 1957. The articles primarily present recent developments in high-speed research, including heat transfer at extreme temperatures. Approximately half of the papers are devoted to problems in heat transfer, and the remainder to studies in the field of fluid mechanics.

The volume contains 439 pages. The size of type used and the excellent figures included make each paper highly readable. According to a statement in the preface, many of the papers will also be published in the technical journals of the five sponsoring societies—American Institute of Chemical Engineers, American Society of Mechanical Engineers, American Society of Refrigeration Engineers, Institute of the Aeronautical Sciences, and Society of Automotive Engineers.

The purpose of the 1957 Institute was to make available, in the West, a program devoted to advanced fundamental research in heat transfer and fluid mechanics. An inspection of the individual papers indicates that the objective has been attained. The authors of the papers were not necessarily from the West, as is evidenced by a broad geographical distribution within the United States. Several of the authors were from Canada—a fact which reflects the wide interest in the Institute meetings.

David Fultz of the University of Chicago and E. R. G. Eckert of the University of Minnesota were invited to present lectures. The titles of their lectures are listed in the table of contents, but the text material has not been included.

In addition to the five professional societies, the following universities were also cosponsors of the 1957 Institute: California Institute of Technology; Santa Clara University; Stanford University; University of California, Berkeley and Los Angeles; and the University of Southern California.

G. A. HAWKINS

Purdue University

The Exploration of the Colorado River. John Wesley Powell. University of Chicago Press, Chicago, 1957 (abridged from the first edition of 1875). xxi + 138 pp. Illus. $3.75.

John Wesley Powell (1834–1902) was the founder and first director of the Smithsonian Institution's Bureau of Ethnology, second director of the U.S. Geological Survey, and author of the classic *Report on the Lands of the Arid Regions of the United States* (1878). He was also leader of the Geographical and Geological Survey of the Rocky Mountain Region (the Powell Survey), which explored and mapped the Plateau Province in the 1870's.

Powell made his first trip into the Plateau Province in the summer of 1869, when he led the first exploration of the Colorado River, boating down the Green and Colorado from Green River, Wyoming, to the mouth of the Virgin, below Grand Canyon. He made his second journey down the river in two stages in 1871 and 1872, having spent the year 1870 obtaining support and finding accessible crossings where supplies could be cached for his second expedition.

Powell's narrative of his adventures in the canyons of the Green and Colorado, which was published in book form in 1875 as the first part of *Exploration of the Colorado River of the West and Its Tributaries*, is now reprinted, together with some of the original illustrations. The account was originally published serially in *Scribner's Monthly* (1874–75), and it is written as a report of the first trip. However, the account is actually based not only on the first trip but also on the second, and it contains, in addition, the story of Powell's 1870 trip south through Pipe Spring, Arizona, into Grand Canyon, to which in turn is tacked a description of his 1872 journey down Parúnuweap Canyon into what is now Zion National Park. Some may object to this "tampering" with the facts; those who will allow an author some license will enjoy the book for what it is, a good story of "white-water" boating in unknown waters in heavy, cumbersome craft.—R.V.O.

Miscellaneous Publications

(Inquiries concerning these publications should be addressed, not to Science, *but to the publisher or agency sponsoring the publication.)*

Records of Oceanographic Works in Japan (Special number for the Oceanographic Research Project by the Japanese National Commission for UNESCO). Compiled by the Pacific Science Liaison Committee of the Science Council of Japan. 208 pp. *Oceanographic Papers in Japan* (Annotated bibliography, 1873–1938). Koji Hidaka *et al.* 235 pp. Japanese National Commission for UNESCO, Tokyo, 1957.

Histology. H. G. Q. Rowett. Rinehart, New York, 1957. 47 pp. $0.95.

Current Medical Research. A reprint of the articles in the report of the Medical Research Council for the year 1955–56. Her Majesty's Stationery Office, London, 1957. 56 pp. 2s. 6d.

The Pseudococcidae (Hom.: Coccoidae), Described by H. C. James, from East Africa. Bulletin, Entomology, vol. 5, No. 5. G. De Lotto. 50 pp. 15s. *A Revision of the Genus Neozephyrus Sibatani and Ito (Lepidoptera: Lycaenidae).* Bulletin, Entomology, vol. 5, No. 6. T. G. Howarth. 40 pp. 15s. British Museum (Natural History), London, 1957.

The Meigs Creek No. 9 Coal Bed in Ohio. pt. III, *Further Study of the Chemical and Physical Properties and Washability Characteristics, with a Brief Review of New Methods Employed.* Bulletin No. 165. Peter O. Krumin. Ohio State University, Columbus, 1957. 373 pp. $3.

Fire Research 1956. Report of Fire Research Board and the report of the Director of Fire Research 50 pp. $0.77. *Food Investigation, 1956.* The report of the Food Investigation Board with the report of the Director of the Food Investigation Organization. 68 pp. $0.68. Department of Scientific and Industrial Research, London, 1957 (order from British Information Services, New York).

The Typical Muscid Flies of California (Diptera: Muscidae, Muscinae). Bulletin of the California Insect Survey, vol. 6, No. 1. Bruce F. Eldridge and Maurice T. James. 17 pp. $0.50. *The Conopid Flies of California (Diptera).* vol. 6, No. 2, Sidney Camras and Paul D. Hurd, Jr. 31 pp. $0.75. *The Embioptera of California.* vol. 6, No. 3. Edward S. Ross. 7 pp. $0.50. University of California Press, Berkeley, 1957.

A New Race of Wood Rat (Neotoma) from the Gulf Side of Central Baja California, Mexico. Transactions, vol. XII, No. 15. Laurence M. Huey. 2 pp. *Late Pleistocene Faunas from the Northwestern Coast of Baja California, Mexico.* vol. XII, No. 16. James W. Valentine. 20 pp. *Type Material of Eucalodium Orcutti Dall (Gastropoda: Pulmonata) from Oaxaca, Mexico.* vol. XII, No. 17. Robert J. Drake. 2 pp. San Diego Society of Natural History, San Diego, 1957.

Le Regime Alimentaire des Poissons du Lac Kivu (Congo Belge et Ruanda). Et l'exploitation des resources naturelles du lac. Exploration hydrobiologique des Lacs Kivu, Edouard et Albert (1952–1954). vol. III, pt. 2, *Resultats Scientifiques.* Jean Verbeke. Institut Royal des Sciences Naturelles de Belgique, Bruxelles, 1957. 221 pp.

Heredo - Retinopathia Congenitalis. Monohybrida Recessiva Autosomalis. A genetical-statistical study. *Hereditas, 43.* Carl Henry Alstrom and Olof Olson. Mendelian Society, 3 Adelgatan, Lund, Sweden, 1957. 178 pp.

Midwest Research Institute, 12th Annual Report of the President to the Trustees. Midwest Research Institute, Kansas City, Mo., 1957. 16 pp.

First Conference on Manufacturing Automation. Purdue University, 22–24 Oct. 1956. Automation, Cleveland, Ohio, 1956. 96 pp.

U.S. Research Reactors. Prepared by Battelle Memorial Institute for U.S. Atomic Energy Commission, Washington, 1957 (order from Office of Technical Services, U.S. Department of Commerce, Washington). 73 pp. $1.50.

Salaries and Earnings of Engineering Teachers 1956. William H. Miernyk and Morris A. Horowitz. American Society for Engineering Education, Urbana, Ill., 1957. 19 pp. $0.25.

The American Heart Association, Proceedings of the 30th Scientific Sessions. 25–28 Oct. 1957. American Heart Assoc., New York, 1957. 128 pp.

The Air Pollution Bibliography. vol. 1. Jack R. Gibson, Wave E. Culver, Mary E. Kurz. Technical Information Division, Library of Congress, Washington 25, 1957. 150 pp.

Meetings and Societies

Preview of Programs at AAAS Indianapolis Meeting

Some of the programs to be presented at the 1957 AAAS meeting in Indianapolis are given here. Others will be announced in subsequent issues.

Mathematics

Section A. Vice-presidential addresses, "Mathematicians in the Market Place," by Mina Rees, Hunter College; and "Mathematical Programming," by A. W. Tucker, Princeton University, 26 Dec., afternoon; C. C. MacDuffee, University of Wisconsin, presiding.

Symposium, cosponsored by the National Council of Teachers of Mathematics and the AAAS Cooperative Committee on the Teaching of Science and Mathematics: "Mathematics Instruction"; arranged by John R. Mayor, American Association for the Advancement of Science, who will preside; 27 Dec., morning. "The Committee on the Undergraduate Program of the Mathematical Association of America," Robert L. Davis, University of Virginia; "The Commission on Mathematics of the College Entrance Examination Board," A. W. Tucker, Princeton University; "The University of Illinois Study on School Mathematics," Max Beberman, University of Illinois; "Mathematics curriculum in perspective," C. C. MacDuffee, University of Wisconsin.

Invited papers: "The Mathematics of Guided Missiles"; 28 Dec., morning; A. W. Tucker, presiding. "Optimal filtering in missile guidance," A. George Carlton, Johns Hopkins University; "Some mathematics and physics of artificial earth satellites," Homer E. Newell, Jr., U.S. Naval Research Laboratory; "Mathematics and ballistic missiles—an overview," Robert W. Rector, Ramo-Wooldridge Corporation.

Association for Computing Machinery. Symposium, cosponsored by Section A: "Computer Research and Applications"; arranged by Jim Douglas, Jr., Rice Institute; 28 Dec., afternoon; Marshall Wrubel, Indiana University, presiding. "Logical engines and education in the sciences," Wallace Givens, Wayne State University; "Development of research effort in the automatic programming of numerically controlled machine tools," Douglas T. Ross, Massachusetts Institute of Technology; "On the design of accelerators and the use of computers by MURA (Midwestern Universities Research Association)," James N. Snyder, University of Illinois; a fourth paper, H. R. J. Grosch, General Electric Company.

National Council of Teachers of Mathematics. Invited papers, cosponsored by Section A: "The Teaching of Mathematics"; arranged by Philip Peak, Indiana University; 27 Dec., afternoon; Marie Wilcox, Howe High School, Indianapolis, Ind., presiding. "The mathematics of the stars," Marshall Wrubel; "Progress report on the Curriculum Study of the Commission on Mathematics," A. W. Tucker; "Progress report on the Curriculum Study of the National Council of Teachers of Mathematics," Lynwood Wren, George Peabody College for Teachers.

Physics

Section B. All symposia are being cosponsored by Sigma Pi Sigma: "Wavelength Standards and Problems of Vacuum Ultraviolet Spectroscopy"; arranged by K. W. Meissner, Purdue University, who will preside; 27 Dec., morning. "The future primary standard of length," K. W. Meissner; "Secondary standards of wavelength," William F. Meggers, National Bureau of Standards; "Recent progress in vacuum ultraviolet spectroscopy," P. G. Wilkinson, University of Chicago; "Lamb shifts in hydrogen and helium," G. Herzberg, National Research Council of Canada; "Solar spectrum in the vacuum ultraviolet," R. Tousey, Naval Research Laboratory.

Vice-presidential address, "Reminiscences in Spectroscopy," by William F. Meggers, 27 Dec., evening; Raymond T. Birge, University of California, presiding.

Symposium: "Spectra of Lanthanides and Actinides: Isotope Shift," arranged by K. W. Meissner; 28 Dec., morning; Raymond T. Birge, University of California, presiding. "Special techniques for the investigation of the spectra of lanthanides and actinides," Frank S. Tomkins, Argonne National Laboratory; "Spectra of rare earths—a challenge to spectroscopists," Charlotte M. Sitterly, National Bureau of Standards; "The spectra of the actinides," Mark Fred, Argonne National Laboratory; "Isotope shift for elements near the middle of the periodic table," Julian E. Mack, University of Wisconsin.

Symposium: "Theory of Spectra: Applied Spectroscopy"; arranged by K. W. Meissner; 28 Dec., afternoon; William F. Meggers, presiding. "Electronic configurations, states, and spectra of some diatomic molecules," R. S. Mulliken, University of Chicago; "Recent progress in the theory of atomic spectra," F. Rohrlich, State University of Iowa; "The role of spectroscopy in thermonuclear research," J. Rand McNally, Jr., Oak Ridge National Laboratory; "Emission spectroscopic determination of oxygen, nitrogen, and hydrogen in metals," V. A. Fassel and W. A. Gordon, Iowa State College.

Symposium: "Some Recent Advances in Physics"; arranged by J. H. McMillen, National Science Foundation; 28 Dec., afternoon; Allan C. G. Mitchell, Indiana University, presiding. "The role of the neutrino in physics," Frederick Reines, Los Alamos Scientific Laboratory; "Some recent advances in solid state physics," Park H. Miller, General Dynamics; "High-temperature plasmas," Alan C. Kolb, Naval Research Laboratory.

Chemistry

Section C. Contributed papers; 27 Dec., morning; Ed F. Degering, Quartermaster Research and Development Laboratories, presiding.

Two-session symposium: "Acetylene Chemistry"; arranged by G. F. Hennion, University of Notre Dame, who will preside; 28 Dec., morning and afternoon. Part I: "Introductory remarks," G. F. Hennion; "Commercial acetylene production," C. K. McLane, Linde Company; "Acetylenic carbinols," G. F. Hennion; "Acetylene derivatives as hydrochloric acid corrosion inhibitors," R. F. Monroe, Dow Chemical Company; "Agricultural uses for acetylene derivatives," Fred J. Lowes, Dow Chemical Company. Part II: "A review of the pharmacology of acetylenic compounds," William R. Gibson, Eli Lilly and Company; "The stereochemistry of nucleophilic additions to acetylenes," W. E. Truce, M. M. Boudakian, J. A. Simms, R. F. Heine, and R. Kassinger, Purdue University; "The acetylene-allene rearrangement," Thomas L. Jacobs, University of California; "Acetylene in the synthesis of pyridines," W. R. Wheeler and F. A. Karnatz, Reilly Tar & Chemical Corporation.

Two-session symposium: "Pyridine Chemistry"; arranged by F. E. Cislak, Reilly Tar & Chemical Corporation,

who will preside; 29 Dec., morning and afternoon. Part I: "Introductory remarks," F. E. Cislak; "Recovery of pyridine from coal products," J. H. Wells, United States Steel Corporation; "The chemistry of vinylpyridines," Robert Levine, University of Pittsburgh; "Derivatives of vinylpyridine," Allan P. Gray, Irwin, Neisler & Company; "Pyridine-metal salt complexes for clathration separation of aromatic isomers," W. D. Schaeffer, W. S. Dorsey, D. A. Skinner, and C. G. Christian, Union Oil Company of California. Part II: "The synthesis and reactions of sterically hindered pyridine bases," Harold Podall, Ethyl Corporation, and Herbert C. Brown, Purdue University; "Chemistry of pyridine-N-oxide," E. C. Taylor, Jr., Princeton University; "Preparation of the pyridolacetones and the inductive effect of nitrogen on the dehydration of the intermediate aldols," John K. Stille, State University of Iowa, and C. S. Marvel, University of Illinois; "Pyrophthalones derived from picolines as intermediates for medicinal agents," C. H. Tilford and G. L. Krueger, William S. Merrell Company, and E. D. Amstutz, D. G. Manly, A. Richardson, Jr., and A. M. Stock, Lehigh University; "The chemistry of picolines," F. E. Cislak.

American Association of Clinical Chemists. General session I; 27 Dec., morning; Donald E. Bowman, Indiana University, presiding.

Annual dinner and speaker: Michael Somogyi, Jewish Hospital of St. Louis.

Symposium: "Significant Trends in the Chemistry of Disease"; arranged by Alfred H. Free, Miles-Ames Research Laboratory, who will preside; 28 Dec., morning, "Electrolytes and acid-base balance," Harry Weisberg, Chicago Medical School and the Little Company of Mary Hospital; "Chemical changes involved in the use of artificial organs," Jack R. Leonards, Western Reserve University Medical School; "Recent advances in the understanding of hormonal factors in disease," Ralph I. Dorfman, Worcester Foundation for Experimental Biology; "Use of serum transaminase activities in clinical biochemistry," Clarence Cohn, Michael Reese Hospital.

General session II; 28 Dec., afternoon; Oliver H. Gaebler, Henry Ford Hospital, presiding

Astronomy

American Astronomical Society. Astronomers' Dinner and address of retiring vice president of Section D: "Facets of Astronomy," by Peter van de Kamp, Swarthmore College; 28 Dec., evening.

Symposium, with Section D: "The Cepheid Variable Stars"; 29 Dec., afternoon; Allan R. Sandage, Mount Wilson and Palomar Observatories, presiding. "Cepheid variables in the small Magellanic cloud," Halton C. Arp, Mount Wilson and Palomar Observatories; "Photoelectric photometry of southern cepheids," John Irwin Goethe Link Observatory; "The spectra of the cepheids in the two stellar populations," Robert Kraft, Goethe Link Observatory; "Comments on the present status of the pulsation theory," Charles Whitney, Smithsonian Astrophysical Observatory.

Helen B. Warner Lecture, joint with Section D: "Unsolved Problems in the Quest for the Extragalactic Scale," by Allan R. Sandage; 29 Dec., evening.

Astronomical League. General meeting, cosponsored by the Indiana Astronomical Society; 26 Dec., afternoon; arranged by Wilhelm Garnatz.

Geology and Geography

Section E. Contributed papers, joint session with the Association of American Geographers, East Lakes and West Lakes Divisions, and the Geological Society of America; 27 Dec., morning; Alfred H. Meyer, Valparaiso University, presiding.

Vice-presidential address, "Uranium Emplacement in the Colorado Plateau,"

by Paul F. Kerr, Columbia University; Robert R. Schrock, Massachusetts Institute of Technology, presiding; followed by Section E Smoker; 27 Dec., evening. Four-session symposium, joint with the Association of American Geographers, East Lakes and West Lakes Divisions, and the Geological Society of America: "Continental Glaciation and Its Geographic Importance as an Environmental Factor"; 28 Dec., morning and afternoon, and 29 Dec., morning and afternoon; Parts I–IV arranged by Frank C. Whitmore, Jr., and Louis L. Ray, U.S. Geological Survey. Part I, William D. Thornbury, Indiana University, presiding. "Present status of glacial geology in Indiana," William D. Thornbury; "Glacial deposits of central and western Ohio," Jane L. Forsyth, Ohio Geological Survey; "Wisconsin glacial deposits of northeastern Ohio," George W. White, University of Illinois; "Present status of glacial geology in Illinois," M. M. Leighton, Illinois Geological Survey; "Present status of glacial geology in Michigan," W. N. Melhorn, Purdue University. Part II, George W. White, University of Illinois, presiding. "Glacial deposits of northwestern Pennsylvania," George W. White and J. B. Droste, Indiana University, R. F. Sitler, Kent State University, and V. C. Shepps, Pennsylvania Geological Survey; "Glacial geology of western and central New York," Ernest H. Muller, Cornell University; "Wisconsin glaciation of the Indianapolis, Indiana, area," Philip W. Harrison, Indiana Geological Survey; "Problems along the margin of the Wisconsin drift in Putnam County, west and central Indiana," C. L. Bieber, DePauw University; "Buried valley systems in parts of northeastern Ohio," John D. Winslow, U.S. Geological Survey; "Pre-Wisconsin peat in Millbury, Massachusetts," Richard J. Lougee, Clark University; "Petrography of Wisconsin tills in oriented sections," Robert F. Sitler, Kent State University. Part III, Paul B. Sears, Yale University, presiding. "Indiana's probable climate during the glacial period," Stephen S. Visher, Indiana University; "Pleistocene climatic change recorded by ice-wedge polygon casts of Cary age at River Falls, Wisconsin," Robert F. Black, University of Wisconsin; "Pleistocene-Wisconsin deposits and soils of Upper Whitewater Basin, Indiana–Ohio," James Thorp, Ansel M. Gooding, and Erling S. Gamble, Earlham College; "Interglacial and late-glacial vegetation of the north central United States," William S. Benninghoff, University of Michigan; "Postglacial vegetation of the north central United States," Theodor Just, Chicago Natural History Museum; "Late Pleistocene biotic changes in Indiana," William J. Wayne, Indiana Geological Survey. Part IV, Louis O. Quam, Office of Naval Research, presiding. "Subsurface sources

of water in the glacial drift of Indiana," Claude M. Roberts, U.S. Geological Survey; "Glacial deposits: a major source of groundwater in the central United States," George B. Maxey and James E. Hackett, Illinois Geological Survey; "Sand and gravel resources of Indiana," Robert L. Schuster, Purdue University; "Glaciers and human activities," Charles G. Morrison, American Geographical Society.

Two-session symposium, jointly with the Geological Society of America: "Mississippian and Pennsylvanian Rocks of the Midwest"; 28 Dec., morning and afternoon; arranged by Henry H. Gray, Indiana Geological Survey, and David H. Swann, Illinois Geological Survey, both of whom will preside. Part I. "Pennsylvanian rocks and basal unconformity in Wayne County, Ohio," H. G. Multer, College of Wooster; "Distinguishing features of Chester and Lower Pennsylvanian rocks in the Illinois Basin," Elwood Atherton, Grover H. Emrich, Herbert D. Glass, Paul E. Potter, and David H. Swann, Illinois Geological Survey; "Stratigraphy of Renault limestone and 'Basin aux Vases' in Indiana subsurface," Arthur P. Pinsak, Indiana Geological Survey; "A correlation and structural interpretation of the Missourian and Virgilian series in southwestern Iowa," T. L. Welp, Iowa State Highway Commission, and L. A. Thomas, Iowa State College; "Late Pennsylvanian facies of north central Oklahoma," Carl C. Branson, University of Oklahoma; "Pennsylvanian conglomerates and tectonic history of the Arbuckle Mountain region," William E. Ham, Oklahoma Geological Survey; "Pennsylvanian history of the Criner Hills area," E. A. Frederickson, University of Oklahoma; "Mississippian stratigraphy and tectonics of the Oklahoma Ozark area," George G. Huffman, University of Oklahoma; "The relationships of the Waynesburg, Hockingport, and Antiquity sandstones of the Dunkard Basin," Wayne D. Martin and William I. Mushake, Miami University, Ohio. Part II. "Crossbedding and sandstone trends in the Chester rocks of the Illinois Basin," Paul E. Potter, Illinois Geological Survey, Edmund Nosow, Kentucky Geological Survey, Ned E. Smith, Indiana Geological Survey, David H. Swann, Illinois Geological Survey, and Frank H. Walker, Kentucky Geological Survey; "Types of Pennsylvanian channel sandstones in Indiana," S. A. Friedman, Indiana Geological Survey; "Geology and petrology of the Anvil rock sandstone of the Illinois Basin," M. E. Hopkins, University of Tulsa, and P. E. Potter and J. A. Simon, Illinois Geological Survey; "Pennsylvanian limestone textures in southwestern Illinois," Russell B. Lennon, Shell Oil Company, and Harold R. Wanless, University of Illinois; "Postulates employed in a Pennsylvanian paleoecological study," Eugene S. Richardson, Jr., and Rainer Zangerl, Chicago Natural History Museum; "Desmoinesian Brachiopoda and Mollusca from southwest Missouri," Richard D. Hoare, Bowling Green State University; "Upper Mississippian and Lower Pennsylvanian megaspores," Marcia R. Winslow, Illinois Geological Survey; "Mississippian smaller Foraminifera of east-central United States," James E. Conkin, University of Louisville; "Arenaceous Foraminifera from the Rockford limestone of northern Indiana," R. C. Gutschick and John Treckman, University of Notre Dame; "The genus *Agassizocrinus* as a stratigraphic marker," R. C. Gutschick, University of Notre Dame, and Edmund Nosow, Kentucky Geological Survey.

Symposium, jointly with the National Speleological Society and the Geological Society of America: "Karst Phenomena"; 30 Dec., morning; arranged by William E. Davies, U.S. Geological Survey, who will preside. "Karst areas of the United States," George W. Moore, Yale University; "Geomorphic aspects of karst," William E. Davies; "Karst features of Swago Creek area, West Virginia," William B. White, Mellon Institute for Industrial Research; "Pseudokarst of the western United States," William R. Halliday, Seattle, Washington; "Pitdome complex in Flint Ridge, Kentucky," R. A. Watson, Cave Research Foundation, Inc.

National Geographic Society. Annual lecture and color film: "The *Bounty* and Pitcairn Island," by Luis Marden, National Geographic Magazine; 29 Dec., evening; Paul A. Scherer, Carnegie Institution of Washington, presiding.

National Speleological Society. Contributed papers, 28 Dec., morning.

Symposium: "Cave Fauna of the Ohio River Valley"; arranged by Thomas C. Barr, Jr., Texas Technological College; 28 Dec., afternoon. "Cave harvestmen (Phalangodidae) of the Ohio River Valley," Clarence J. Goodnight, Purdue University; "Millipedes from Tennessee caves," Nell B. Causey, University of Arkansas; "Cavernicolous pselaphid beetles of the Ohio River Valley," Orlando Park, Northwestern University; "Anophthalmid beetles of southern Indiana," Carl H. Krekeler, Valparaiso University; "Cavernicolous anophthalmid and silphid beetles from Tennessee and Kentucky caves," Thomas C. Barr, Jr.

Forthcoming Events

December

13–14. Association for Research in Nervous and Mental Disease, 37th annual, New York, N.Y. (R. J. Masselink, 700 W. 168 St., New York 32.)

15–18. American Soc. of Agricultural Engineers, Chicago, Ill. (J. L. Butt, ASAE, St. Joseph, Mich.)

16–18. Air Traffic Control Symp., Philadelphia, Pa. (Air Traffic Symp., Franklin Inst. Labs., 20th St. and Parkway, Philadelphia 3.)

17–19. Nuclear Sizes and Density Distributions Conference, Stanford, Calif. (R. Hofstadter, Stanford Univ., Stanford, Calif.)

19–21. American Physical Soc., Stanford, Calif. (W. A. Nierenberg, Univ. of California, Berkeley 4.)

26–27. Northwest Scientific Assoc., annual, Spokane, Wash. (W. B. Merriam, Geography Dept., State College of Washington, Pullman.)

26–30. American Assoc. for the Advancement of Science, annual, Indianapolis, Ind. (R. L. Taylor, AAAS, 1515 Massachusetts Ave., NW, Washington 5.)

The following 44 meetings are being held in conjunction with the AAAS annual meeting.

AAAS Acad. Conference, annual (Father P. H. Yancey, Spring Hill College, Mobile, Ala.). 28 Dec.

AAAS Cooperative Committee on the Teaching of Science and Mathematics (F. B. Dutton, Dept. of Chemistry, Michigan State Univ., East Lansing). 27 Dec.

Alpha Epsilon Delta (M. L. Moore, 7 Brookside Circle, Bronxville, N.Y.). 28 Dec.

American Astronomical Soc. (J. A. Hynek, Smithsonian Astrophysical Observatory, 60 Garden St., Cambridge 38, Mass.). 27–30 Dec.

American Geophysical Union (E. M. Brooks, Dept. of Geophysics, St. Louis Univ., St. Louis 8, Mo.).

American Medical Assoc. Committee on Cosmetics (Mrs. V. L. Conley, AMA, 535 N. Dearborn St., Chicago, Ill.). 28–29 Dec.

American Meteorological Soc. (K. C. Spengler, AMS, 3 Joy St., Boston, Mass.).

American Nature Study Soc., annual (R. L. Weaver, School of Natural Resources, Univ. of Michigan, Ann Arbor). 26–30 Dec.

American Physiological Soc. (F. A. Hitchcock, Dept. of Physiology, Ohio State Univ., Columbus 10.)

American Political Science Assoc. (C. S. Hyneman, Dept. of Government, Indiana Univ., Bloomington). 29 Dec.

American Psychiatric Assoc. (M. Greenblatt, Massachusetts Mental Health Center, 74 Fenwood Rd., Boston 15). 29–30 Dec.

American Soc. of Hospital Pharmacists (G. E. Archambault, Pharmacy Branch, U.S. Public Health Service, Washington 25).

American Soc. of Naturalists (B. Wallace, Biological Lab., Cold Spring Harbor, Long Island, N.Y.).

American Sociological Soc. (V. H. Whitney, Brown Univ., Providence, R.I.). 28 Dec.

American Statistical Assoc. (V. L. Anderson, Statistical Lab., Purdue Univ., Lafayette, Ind.).

Association of American Geographers (L. L. Ray, U.S. Geological Survey, Washington 25).

Association for Computing Machinery (J. E. Robertson, Digital Computer Lab., Univ. of Illinois, Urbana).

Astronomical League (W. Garnatz 2506 South East St., Indianapolis).

Beta Beta Beta (Mrs. F. G. Brooks, P.O. Box 336, Madison Sq. Station, New York 10). 27 Dec.

Biometric Soc., ENAR (T. A. Bancroft, Dept. of Statistics, Iowa State College, Ames).

Conference on Scientific Editorial Problems, annual (G. L. Scielstad, Applied Physics Lab., Johns Hopkins Univ., Silver Spring, Md.). 26–30 Dec.

Conference on Scientific Manpower, annual (T. J. Mills, National Science Foundation, Washington 25). 30 Dec.

Ecological Soc. of America (A. A. Lindsey, Dept. of Biological Sciences, Purdue Univ., Lafayette, Ind.). 27–29 Dec.

Metric Assoc. (J. T. Johnson, 694 West 11 St., Claremont, Calif.).

National Acad. of Economics and Political Science (D. P. Ray, Hall of Government, George Washington Univ., Washington, D.C.).

National Assoc. of Biology Teachers, annual (Miss I. Hollenbeck, Southern Oregon College of Education, Ashland). 26–31 Dec.

National Assoc. for Research in Science Teaching (G. G. Mallinson, Western Michigan College, Kalamazoo). 26–30 Dec.

National Assoc. of Science Writers (J Troan, *Pittsburgh Press,* Pittsburgh, Pa.).

National Council of Teachers of Mathematics (P. Peak, College of Education, Indiana Univ., Bloomington). 27 Dec.

National Foundation for Junior Museums (J. R. Forbes, NFJM, 114 E. 30 St., New York 16). 26, 28 Dec.

National Geographic Soc. (W. R. Gray, NCS, 16th and M Sts., NW, Washington 6). 29 Dec.

National Science Teachers Assoc. (R. W. Schulz, Emmerich Manual Training High School, 2405 Madison Ave., Indianapolis 25). 26–30 Dec.

National Speleological Soc. (Brother G. Nicholas, LaSalle College, 20th and Olney Aves., Philadelphia 41, Pa.) 28 Dec.

Philosophy of Science Assoc. (C. W. Churchman, Case Inst. of Technology, Cleveland, Ohio).

Scientific Research Soc. of America, annual (D. B. Prentice, 56 Hillhouse Ave., New Haven 11, Conn.). 27 Dec.

Sigma Delta Epsilon, annual (Miss M. Chalmers, Dept. of Chemistry, Purdue Univ., Lafayette, Ind.). 26–30 Dec.

Sigma Pi Sigma (M. W. White, Pennsylvania State Univ., University Park). 27 Dec.

Society for the Advancement of Criminology (D. E. J. MacNamara, New York Inst. of Criminology, 40 E. 40 St., New York 16). 27–28 Dec.

Society for General Systems Research, annual (R. L. Meier, Mental Health Research Inst., Ann Arbor, Mich.).

Society for Industrial Microbiology, Washington Section (W. N. Ezekiel, Bureau of Mines, Washington 25).

Society for Investigative Dermatology (H. Beerman, Univ. of Pennsylvania School of Medicine, Philadelphia 3), 28–29 Dec.

Society of the Sigma Xi, annual (T. T.

Holme, 56 Hillhouse Ave., New Haven 11, Conn.). 27 Dec.

Society of Systematic Zoology, annual (R. E. Blackwelder, Box 500, Victor, N.Y.). 26–31 Dec.

United Chapters of Phi Beta Kappa, annual address (C. Billman, 1811 Q St., NW, Washington, D.C.). 27 Dec.

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27. Association for Symbolic Logic., Cambridge, Mass. (J. Barlaz, Rutgers Univ., New Brunswick, N.J.)

27–28. Linguistic Soc. of America, Chicago, Ill. (A. A. Hill, Box 7790, University Station, Austin 12, Tex.)

27–30. American Finance Assoc., annual, Philadelphia, Pa. (G. E. Hassett, Jr., New York Univ., 90 Trinity Pl., New York 6.)

28–29. American Folklore Soc., annual, Chicago, Ill. (M. Leach, Box 5, Bennett Hall, Univ. of Pennsylvania, Philadelphia 4, Pa.)

28–30. American Anthropological Assoc., annual, Chicago, Ill. (W. S. Godfrey, Jr., Logan Museum, Beloit College, Beloit, Wis.)

28–30. American Economic Assoc., annual, Philadelphia, Pa. (J. W. Bell, Northwestern Univ., Evanston, Ill.)

28–30. Archaeological Inst. of America, annual, Washington, D.C. (C. Boulter, 608, Univ. of Cincinnati Library, Cincinnati 21, Ohio.)

28–30. Econometric Soc., Philadelphia, Pa. (R. Ruggles, Dept. of Economics, Yale Univ., New Haven, Conn.)

28–30. History of Science Soc., annual, New York, N.Y. (Miss M. Boas, Brandeis Univ., Waltham 54, Mass.)

January

6–8. Reliability and Quality Control, 4th natl. symp., Washington, D.C. (C. M. Ryerson, RCA Bldg. 10–6, Camden 2, N.J.)

7–10. Radioactive Isotopes in Clinical Application and Research) 3rd internatl. symp., Bad Gastein, Austria. (Second Medical Clinic, Vienna Univ., Vienna, Austria.)

8–10. Northeastern Weed Control Conf., 12th annual, New York. (R. J. Aldrich, Farm Crops Dept., Rutgers Univ., New Brunswick, N.J.)

13–17. Society of Automotive Engineers, annual, Detroit, Mich. (Meetings Div., SAE, 29 W. 39 St., New York 18.)

22–24. American Council of Learned Societies, 39th annual, Bloomington, Ind. (ACLS, 2101 R St., NW, Washington 8.)

22–25. American Group Psychotherapy Assoc., 15th annual, New York. (M. Berger, 50 E. 72 St., New York 21.)

27–28. Scintillation Counter Symp., Washington, D.C. (G. A. Morton, Radio Corporation of America, Princeton, N.J.)

27–29. American Soc. of Heating and Air-Conditioning Engineers, Pittsburgh, Pa. (A. V. Hutchinson, ASHAE, 62 Worth St., New York 13.)

27–30. American Meteorological Soc., 163rd natl., New York. (K. C. Spengler, AMS, 3 Joy St., Boston 8, Mass.)

27–31. Institute of Aeronautical Sciences, 26th annual, New York, N.Y. (S. P. Johnston, IAS, 2 E. 64 St., New York 21.)

28–30. Aging, 4th Ciba Foundation Colloquium (by invitation), London, England. (G. E. W. Wolstenholme, 41 Portland Pl., London, W.1.)

28–30. American Mathematical Soc., 64th annual, Cincinnati, Ohio. (J. H. Curtiss, AMS, 190 Hope St., Providence 6, R.I.)

29–1. American Physical Soc., annual, New York, N.Y. (K. K. Darrow, Columbia Univ., New York 27.)

30–31. College–Industry Conf., American Soc. for Engineering Education, 10th annual, Ann Arbor, Mich. (W. D. McIlvaine, College of Engineering, Ann Arbor.)

30–1. American Assoc. of Physics Teachers, New York. (F. Verbrugge, Univ. of Minnesota, Minneapolis.)

30–1. Western Soc. for Clinical Research, 11th annual, Carmel-by-the-Sea, Calif. (A. J. Seaman, Univ. of Oregon Medical School, Portland 1.)

31. Mathematical Assoc. of America, annual, Cincinnati, Ohio. (H. M. Gehman, Univ. of Buffalo, Buffalo 14, N.Y.)

February

1–14. Pan American Assoc. of Ophthalmology, Caribbean cruise cong., sailing from New York, N.Y. (L. V. Arnold, 33 Washington Sq. W., New York 11.)

3–4. Progress and Trends in Chemical and Petroleum Instrumentation, Wilmington, Del. (H. S. Kindler, Instrument Soc. of America, 313 Sixth Ave., Pittsburgh 22, Pa.)

3–7. American Inst. of Electrical Engineers, winter genl., New York, N.Y. (N. S. Hibshman, AIEE, 33 W. 39 St., New York 18.)

10–14. American Soc. for Testing Materials, St. Louis, Mo. (F. F. Van Atta, ASTM, 1916 Race St., Philadelphia 3, Pa.)

16–20. American Inst. of Mining, Metallurgical and Petroleum Engineers, annual, New York. (E. O. Kirkendall, AIME, 29 W. 39 St., New York 18.)

20–21. Transistor and Solid State Circuits Conf., Philadelphia, Pa. (J. H. Milligan, Jr., Dept. of Electrical Engr., New York Univ., New York 53.)

EQUIPMENT NEWS

The information reported here is obtained from manufacturers and from other sources considered to be reliable. Science *does not assume responsibility for the accuracy of the information. All inquiries concerning items listed should be addressed to* Science, *Room 740, 11 W. 42 St., New York 36, N.Y. Include the name(s) of the manufacturer(s) and the department number(s).*

■ HUMIDITY CONTROLLER maintains constant humidity within ±0.25 percent relative humidity in an air or gas stream. The unit comprises a sensing element, control system, and modulating device. Sizes ranging from one with a capacity of 20 ft^3/min are available. The control point is set by a knob. Operation is accurate in the humidity range from 3 to 98 percent. (Universal Dynamics Corp., Dept. S724)

■ STERILIZER is said to provide complete dry-heat sterilization 5 min after proper temperature has been reached. Trays for equipment, three in number, measure 7¾ by 13¾ in. (Associated Mills, Dept. S729)

■ VACUUM-FUSION APPARATUS provides direct analysis of hydrogen and oxygen in alloys, nitrogen being determined by difference. Both vacuum-fusion and high-temperature extraction can be used. Oxygen analysis is performed in an auxiliary apparatus which connects through a ball-and-socket joint. Oxides in the sample react with graphite to produce CO, which is further oxidized to CO_2 and measured. Hydrogen concentration from 0.1 to 2000 parts per million is measurable. The hydrogen is separated by diffusion through palladium and measured volumetrically. Results are said to be accurate to ±0.2 part per million. (Fisher Scientific Co., Dept. S743)

■ LIQUID-NITROGEN REFRIGERATOR is a special container designed to permit storage baskets filled with material to be lowered into the liquid nitrogen. The unit weighs 115 lb fully charged and 60 lb empty. A single charge of liquid nitrogen will maintain a temperature of −320°F for up to 34 days. (Union Carbide Corp., Dept. S741)

■ ELECTRON ACCELERATOR is designed for use in research on the effects of radiation on chemical, food, drug, and electronic products. High-energy electrons, x-rays, or neutrons are provided as desired. The electron beam is variable in energy from 2 to 10 Mev. Full power is 4 kw. The beam is pulsed, with energy per pulse variable to a maximum of 11 joules. The x-ray dose is variable to 5×10^6 r/min. Maximum total neutron production, through (γ,n) reaction in a beryllium tar-

get, is 10^{11}/sec; maximum thermal neutron flux is 10^9/cm²/sec. The electron beam can be magnetically deflected or scanned to provide a uniform field. (Applied Radiation Corporation, Dept. S740)

■ MOISTURE AND DENSITY METER yields density measurements accurate within 2 lb/ft³ over the range from 50 to 150 lb/ft³; and moisture measurements accurate within 0.75 lb/ft³ from 0 to 100 percent moisture content. Time required for each measurement is 2 min. The instrument operates on the principle that the scattering of gamma radiation is a function of density and that the scattering of neutrons is a function of moisture concentration. Measurement of the scattered radiation provides the required information. The moisture probe contains a radium-beryllium source of fast neutrons; the density probe a cesium-137 gamma source. The probes normally sample a sphere of 14 in. average diameter. Measurements may be made at depths up to 60 ft. (Nuclear Chicago Corp., Dept. S739)

■ AUTOMATIC TITRATION APPARATUS is designed for connection to a plant stream. The apparatus samples the stream at intervals and, under the control of electronic programing instruments, performs a titration with a standard reagent. The volume of reagent used is detected photoelectrically and recorded. The chemical unit in which the analysis is performed and the electronic control unit which determines the sequence of operations are separately housed. The time cycle of titration can be varied from 3 to 30 min. Operation on a 24-hr basis is said to require no attention beyond a routine weekly inspection. (Robertshaw-Fulton Controls Co., Dept. S738)

■ ELECTROLYTIC CONDUCTIVITY RECORDER is battery operated. Chart drive is provided by clockwork. Circuitry has been transistorized to minimize battery drain. Conductivity is recorded on a circular chart by a self-balancing Wheatstone bridge excited at a frequency of 1000 cy/sec. Measurements of electrolytes ranging from distilled water to strong acids can be made. Automatic or manual temperature compensation can be provided. (Industrial Instruments, Inc., Dept. S737)

■ LINEAR AMPLIFIER for use with radiation detectors has input sensitivity of from 200 μv to 1 mv. Linearity is better than 1 percent from 9- to 90-v output. Stability is better than 1 percent after 24-hour warm-up. Gain is variable between 2000 and 12,000, depending on band width. (Victoreen Instrument Co., Dept. S735)

JOSHUA STERN

National Bureau of Standards

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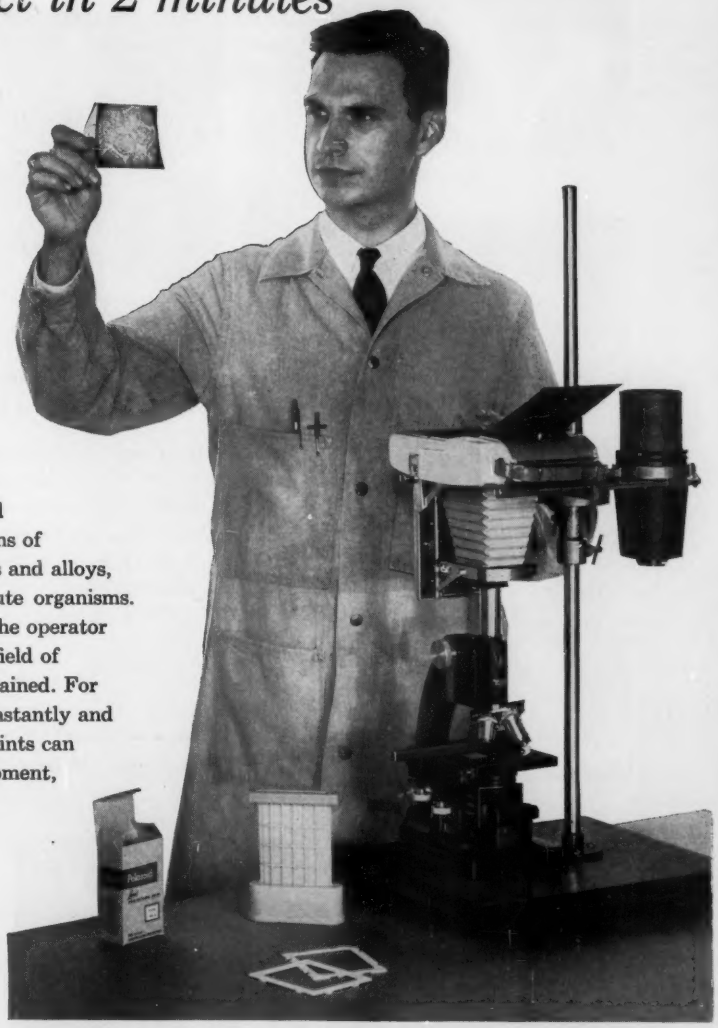

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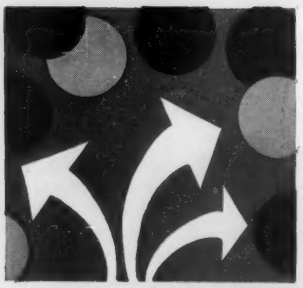

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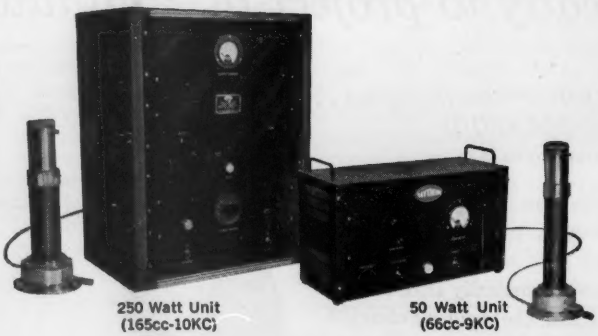

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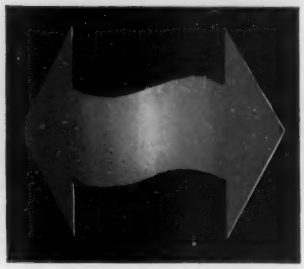

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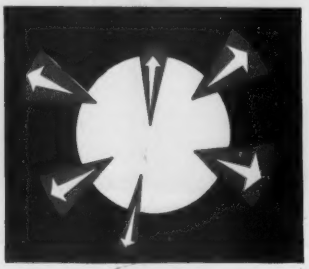

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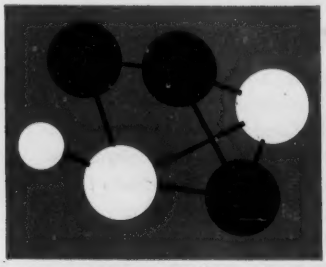

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